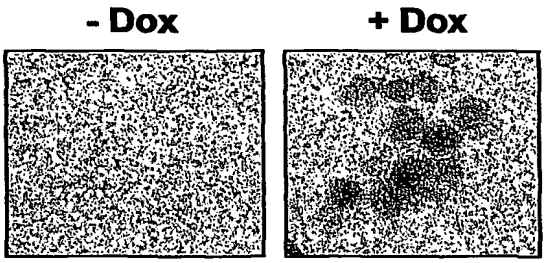


FIG. 1A

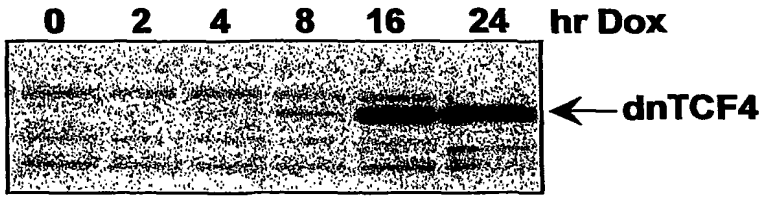


FIG. 1B

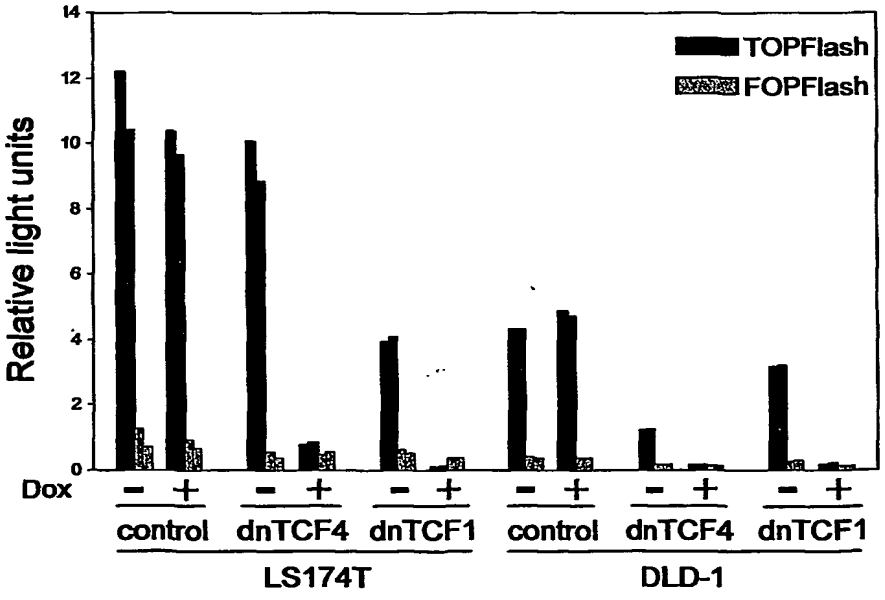


FIG. 1C

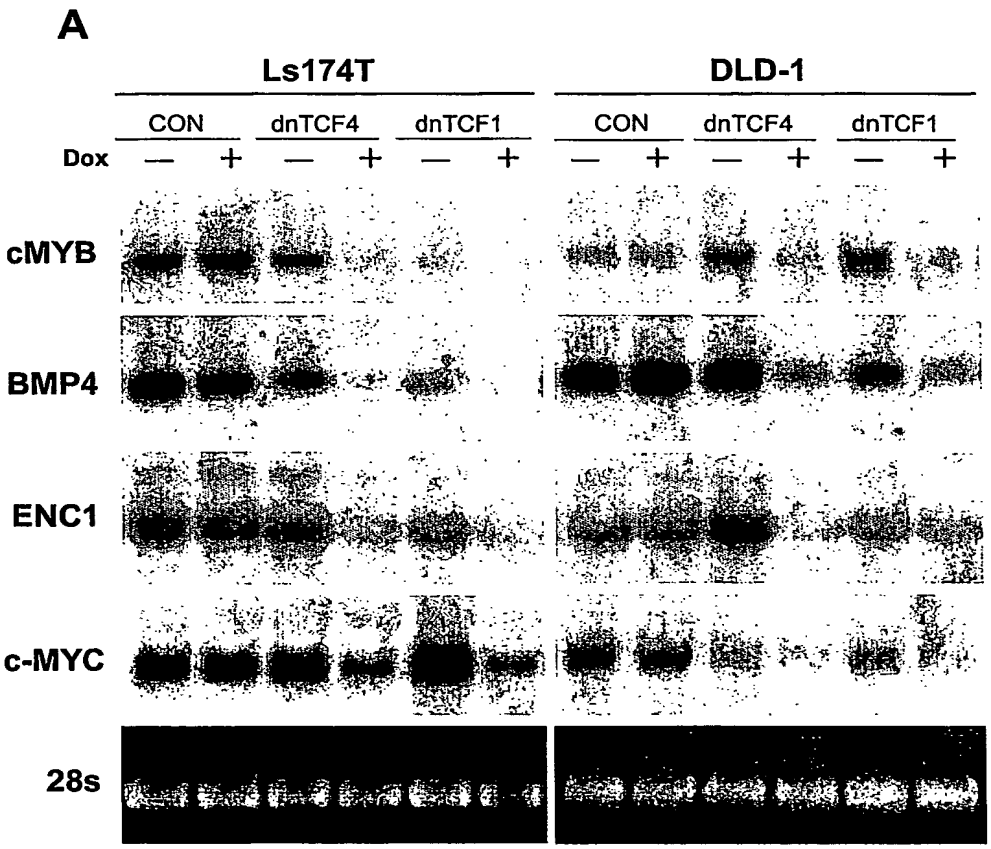
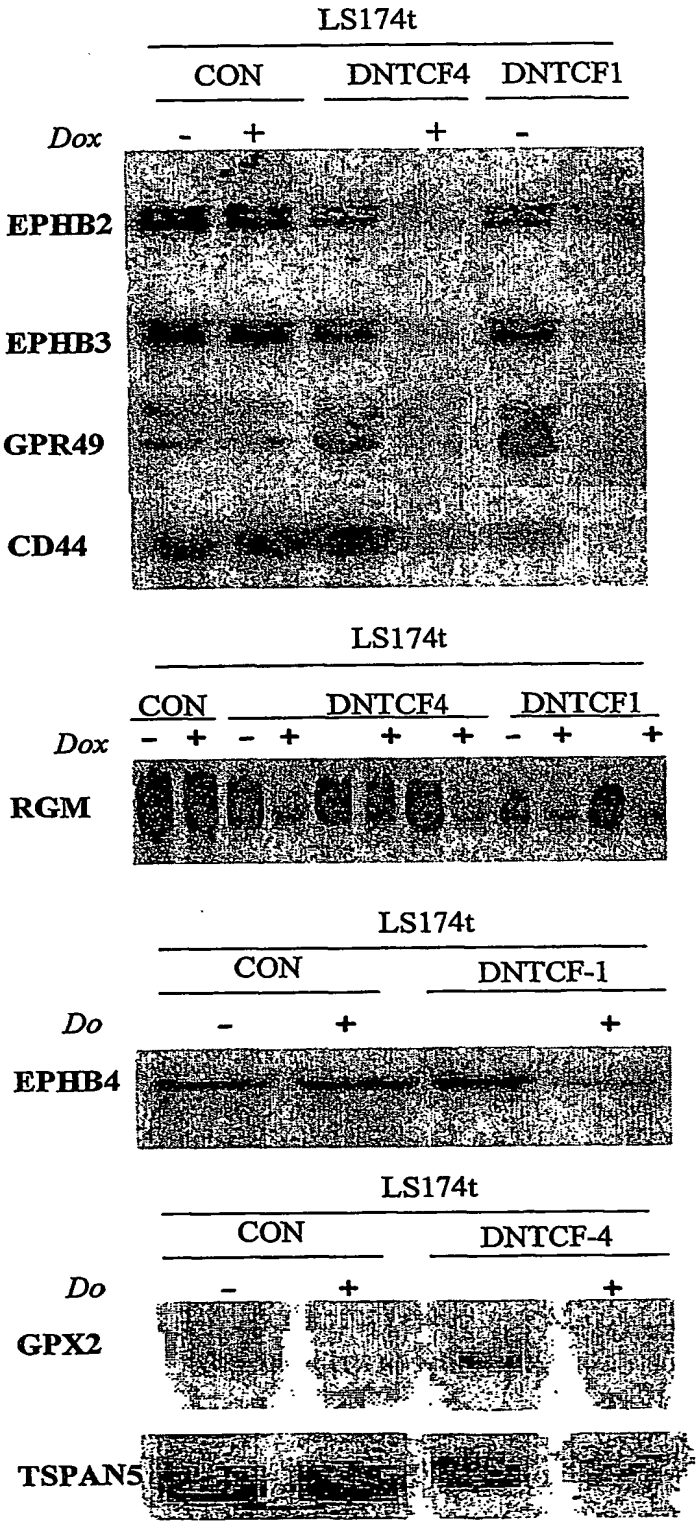

A
Ls174T
DLD-1
CON
dnTCF4
dnTCF1
CON
dnTCF4
dnTCF1
Dox
— + — + — + — + — + — +
cMYB
BMP4
ENC1
c-MYC
28s

FIG. 2A

B)


LS174t
CON
DNTCF4
DNTCF1
Dox
- + + -
EPHB2
EPHB3
GPR49
CD44
LS174t
CON
DNTCF4
DNTCF1
Dox
- + - + + + - + +
RGM
LS174t
CON
DNTCF-1
Do
- + +
EPHB4
LS174t
CON
DNTCF-4
Do
- + +
GPX2
TSPAN5

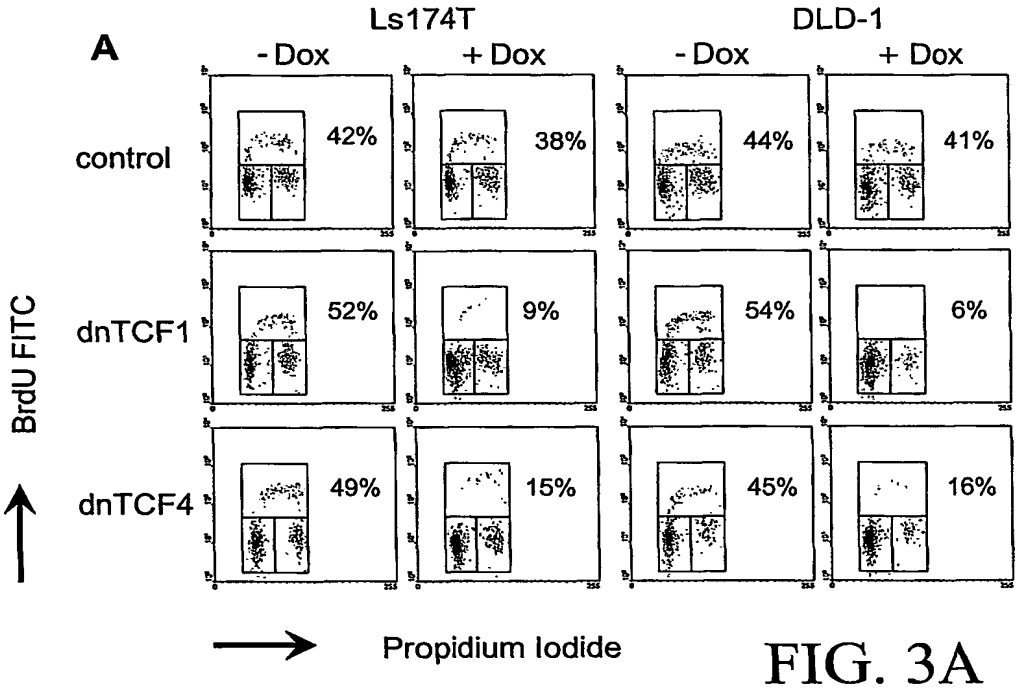

A
Ls174T
DLD-1
- Dox
+ Dox
- Dox
+ Dox
control
dnTCF1
dnTCF4
42%
38%
44%
41%
52%
9%
54%
6%
49%
15%
45%
16%
BrdU FITC
Propidium Iodide

FIG. 3A

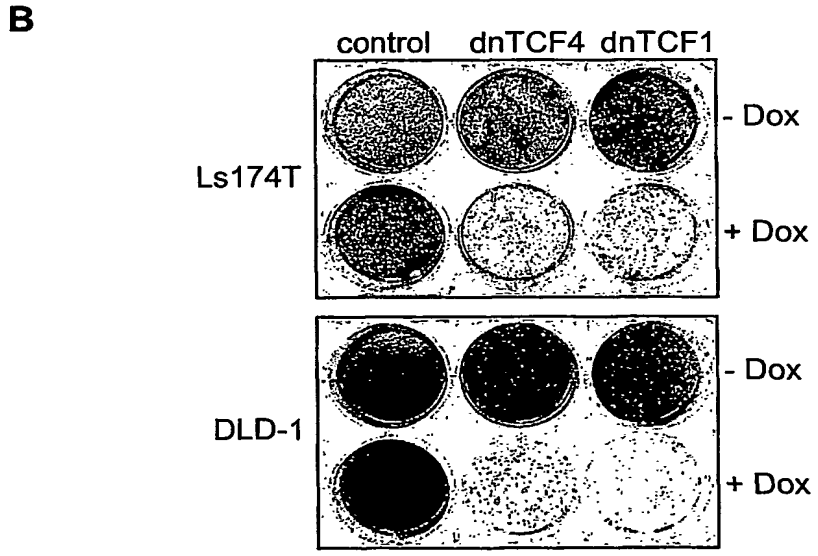

B
control
dnTCF4
dnTCF1
Ls174T
DLD-1
- Dox
+ Dox
- Dox
+ Dox

FIG. 3B

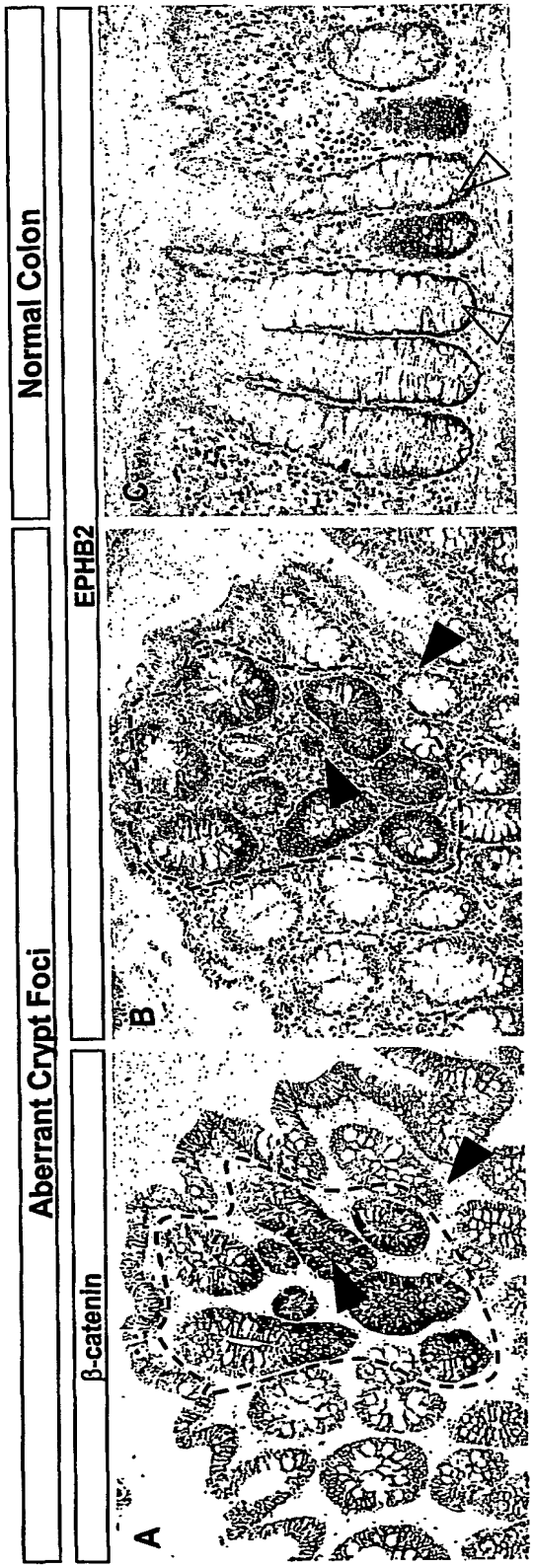


FIG. 4A

FIG. 4B

FIG. 4C

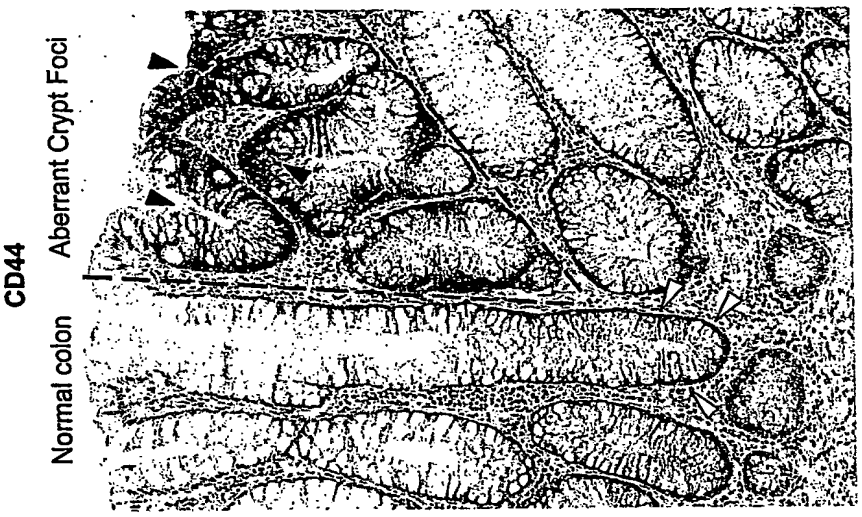

CD44
Aberrant Crypt Foci
Normal colon

FIG. 5B

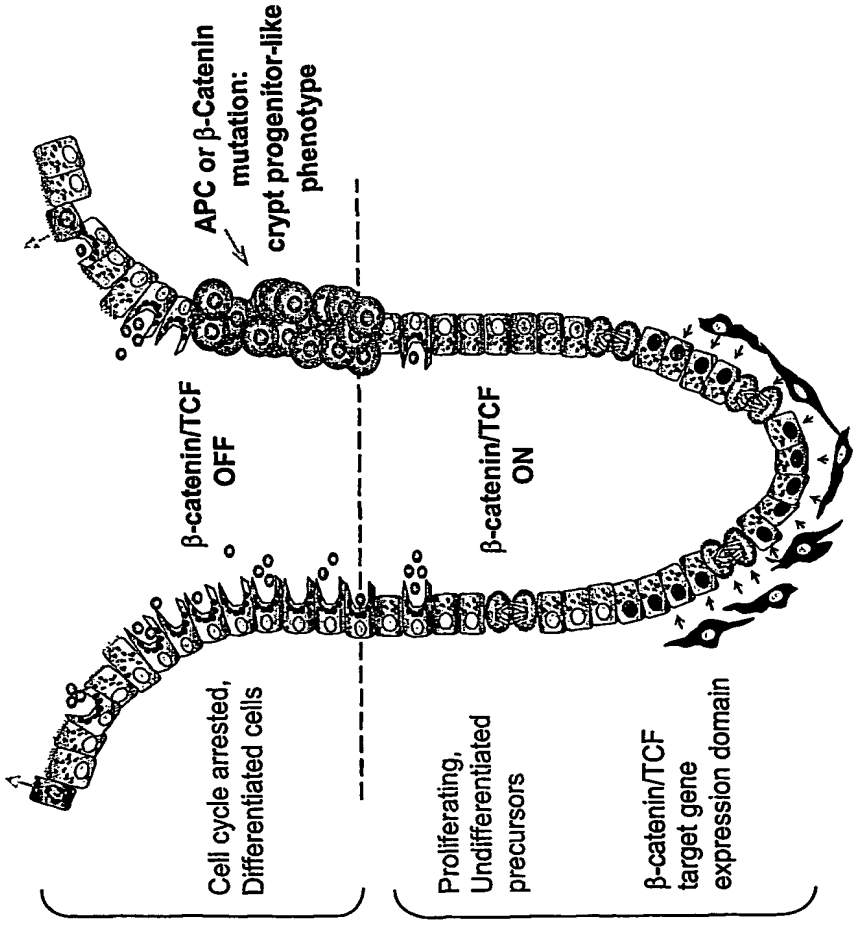

APC or β-Catenin mutation: crypt progenitor-like phenotype
β-catenin/TCF OFF
β-catenin/TCF ON
Cell cycle arrested, Differentiated cells
Proliferating, Undifferentiated precursors
β-catenin/TCF target gene expression domain

FIG. 5A

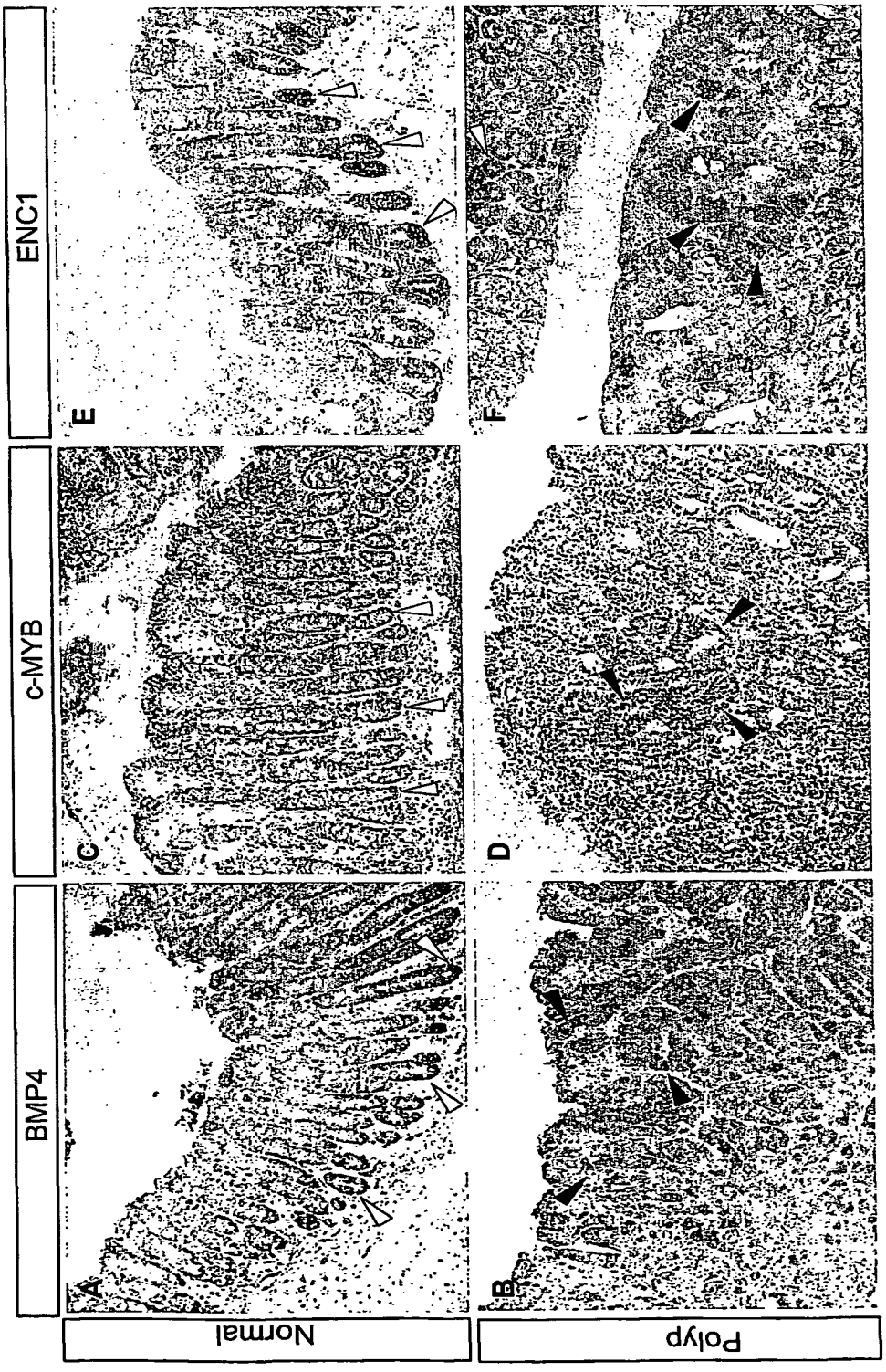


FIG. 6

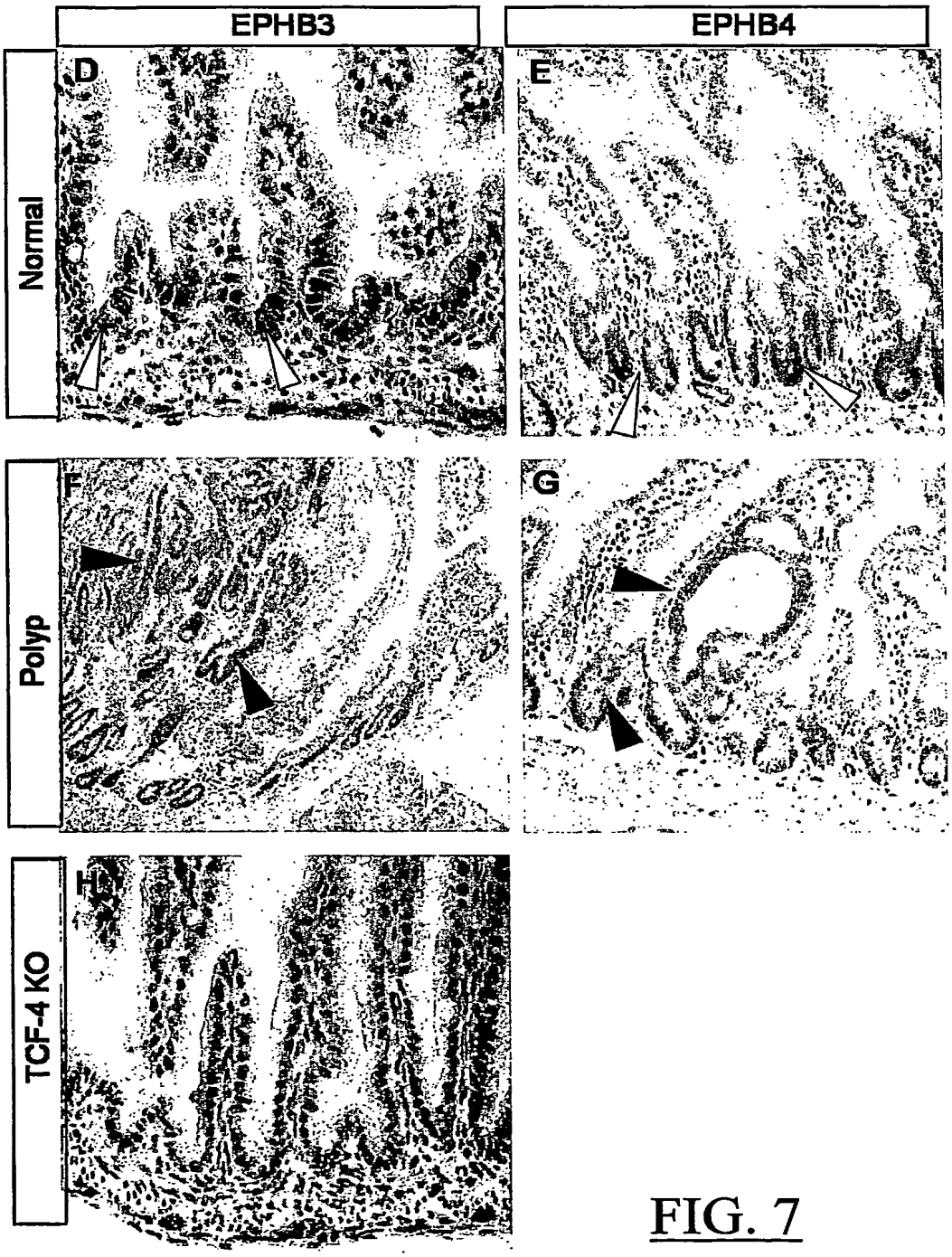


FIG. 7

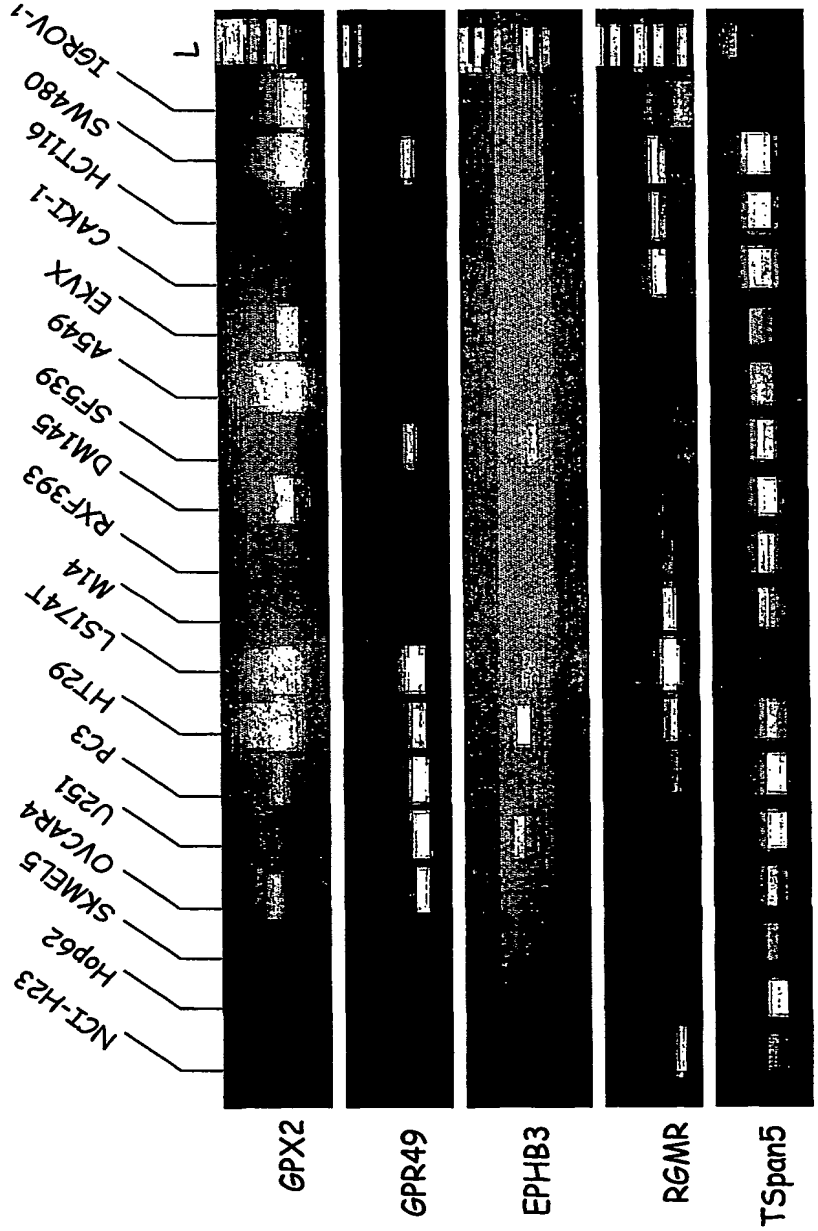

GPX2
GPR49
EPHB3
RGMR
TSpan5
NCI-H23
Hop62
SKMEL5
OVCAR4
U251
PC3
HT29
LS174T
M14
RXF393
DM145
SF539
A549
EKVX
CAKI-1
HCT116
SW480
IGROV-1
L

FIG. 8A

Cancer Type	Cell-Line	GPX2 Expression Level	GPR49 Expression Level	EPHB3 Expression Level	RGMR Expression Level	TSpan 5 Expression Level
Lung	NCI-H23	+	-	+	++	+
	Hop62	+	-	+	+	++
	A549	+++	-	+	+	+
	EKVX	++	-	+	+	+
Ovarian	OVCAR-4	++	++	-	+	+
	IGROV-1	++	-	-	+	-
Central Nervous System	U251	+	+++	++	+	+++
	SF539	-	+	++	-	++
Skin	SKMEL5	-	-	-	+	+
	M14	-	-	+	++	+
Colon	HT29	+++	++	+++	++	+
	LS174T	+++	+++	++	+++	ND
	SW480	++	++	-	+++	+++
	HCT116	+	-	-	++	++
Prostate	PC3	++	+++	-	+	+++
	DM145	++	-	-	+	+++
Kidney	RXF393	-	-	-	+	+
	CAKI-1	-	-	-	+++	++

FIG. 8B

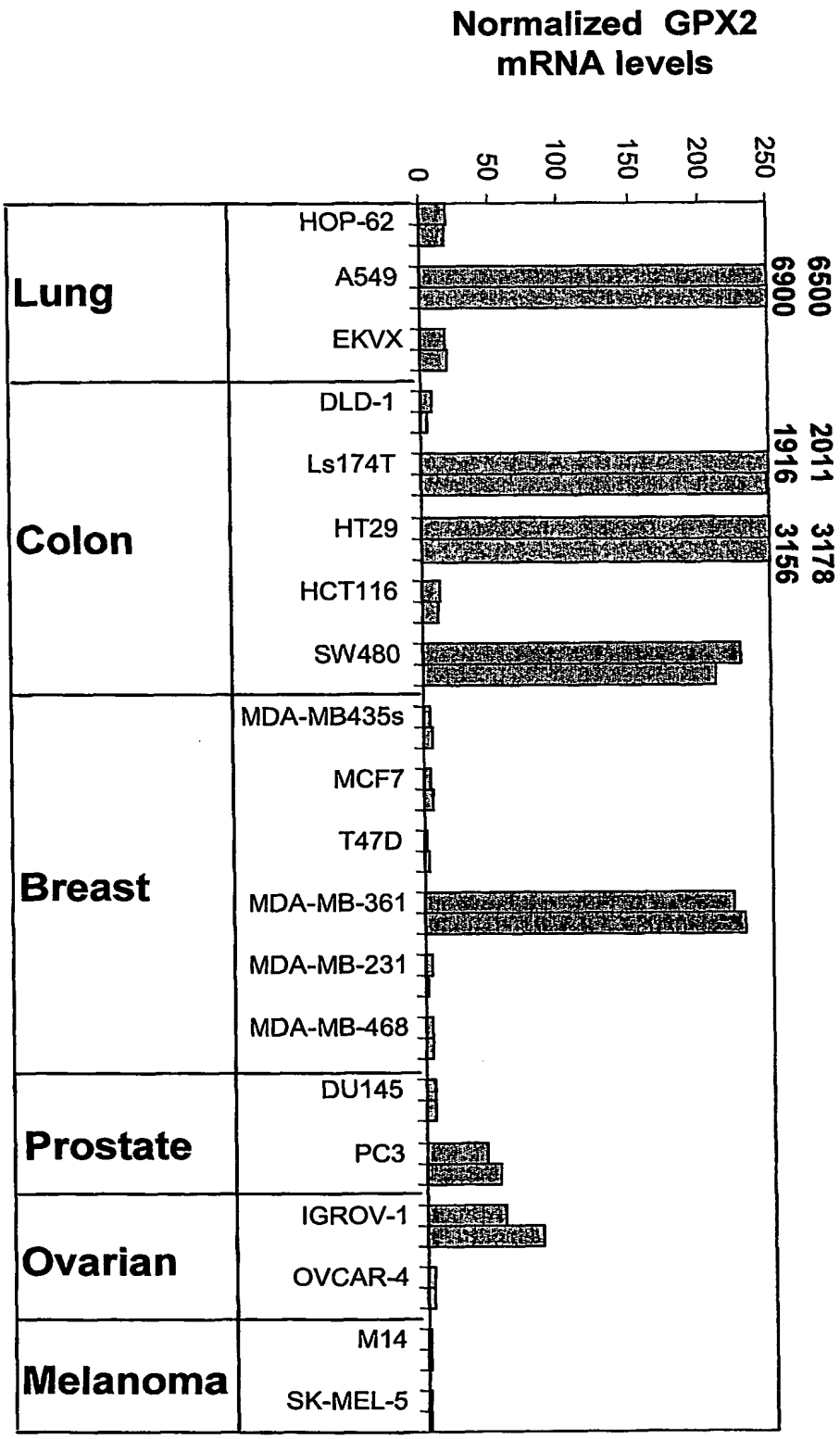

Normalized GPX2 mRNA levels
0
50
100
150
200
250
Lung
HOP-62
A549
EKVX
6500
6900
Colon
DLD-1
Ls174T
HT29
HCT116
SW480
1916
2011
3156
3178
Breast
MDA-MB435s
MCF7
T47D
MDA-MB-361
MDA-MB-231
MDA-MB-468
Prostate
DU145
PC3
Ovarian
IGROV-1
OVCAR-4
Melanoma
M14
SK-MEL-5

FIG. 9A

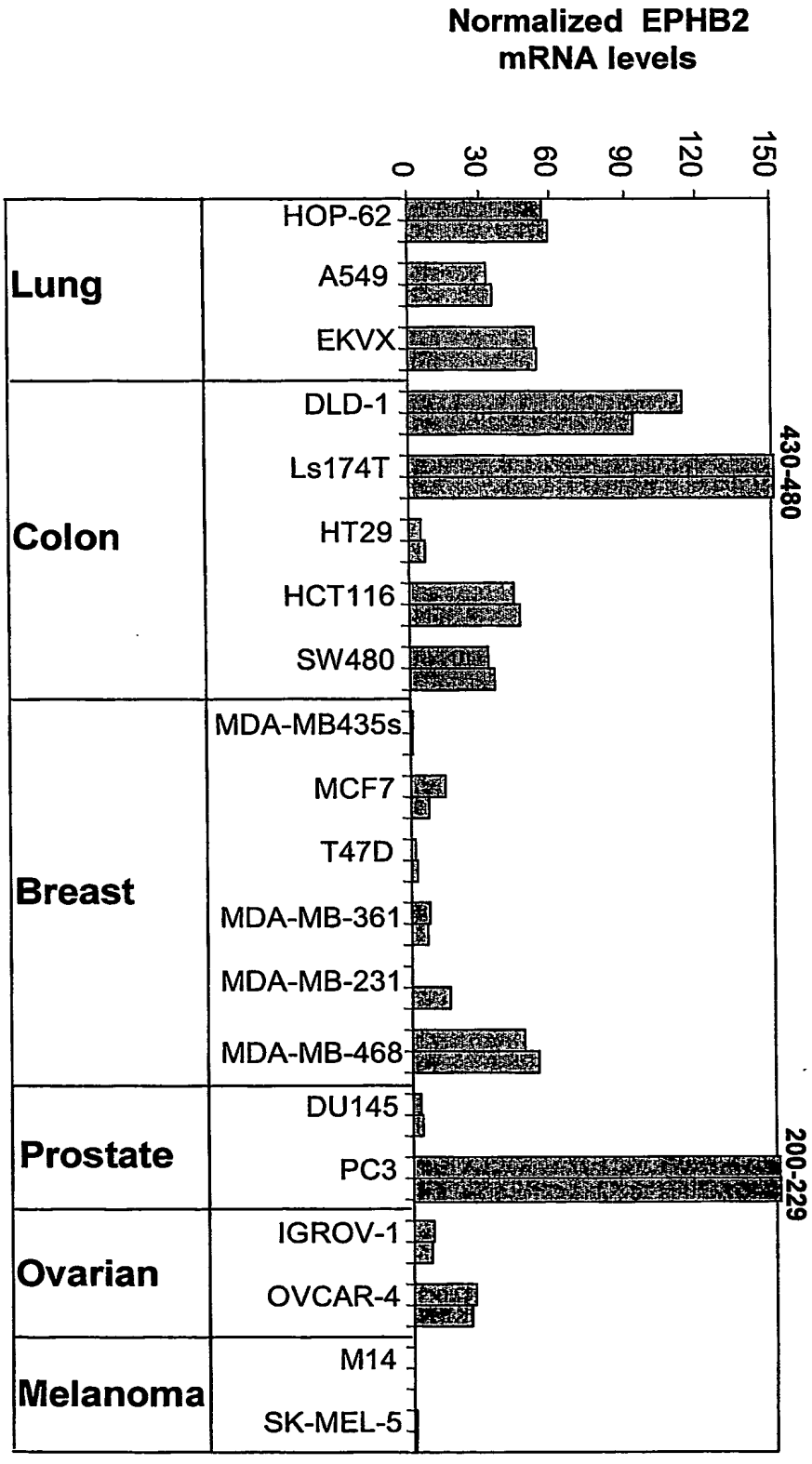

Normalized EPHB2
mRNA levels
0
30
60
90
120
150
Lung
HOP-62
A549
EKVX
Colon
DLD-1
Ls174T
HT29
HCT116
SW480
430-480
Breast
MDA-MB435s
MCF7
T47D
MDA-MB-361
MDA-MB-231
MDA-MB-468
Prostate
DU145
PC3
200-229
Ovarian
IGROV-1
OVCAR-4
Melanoma
M14
SK-MEL-5

FIG. 9B

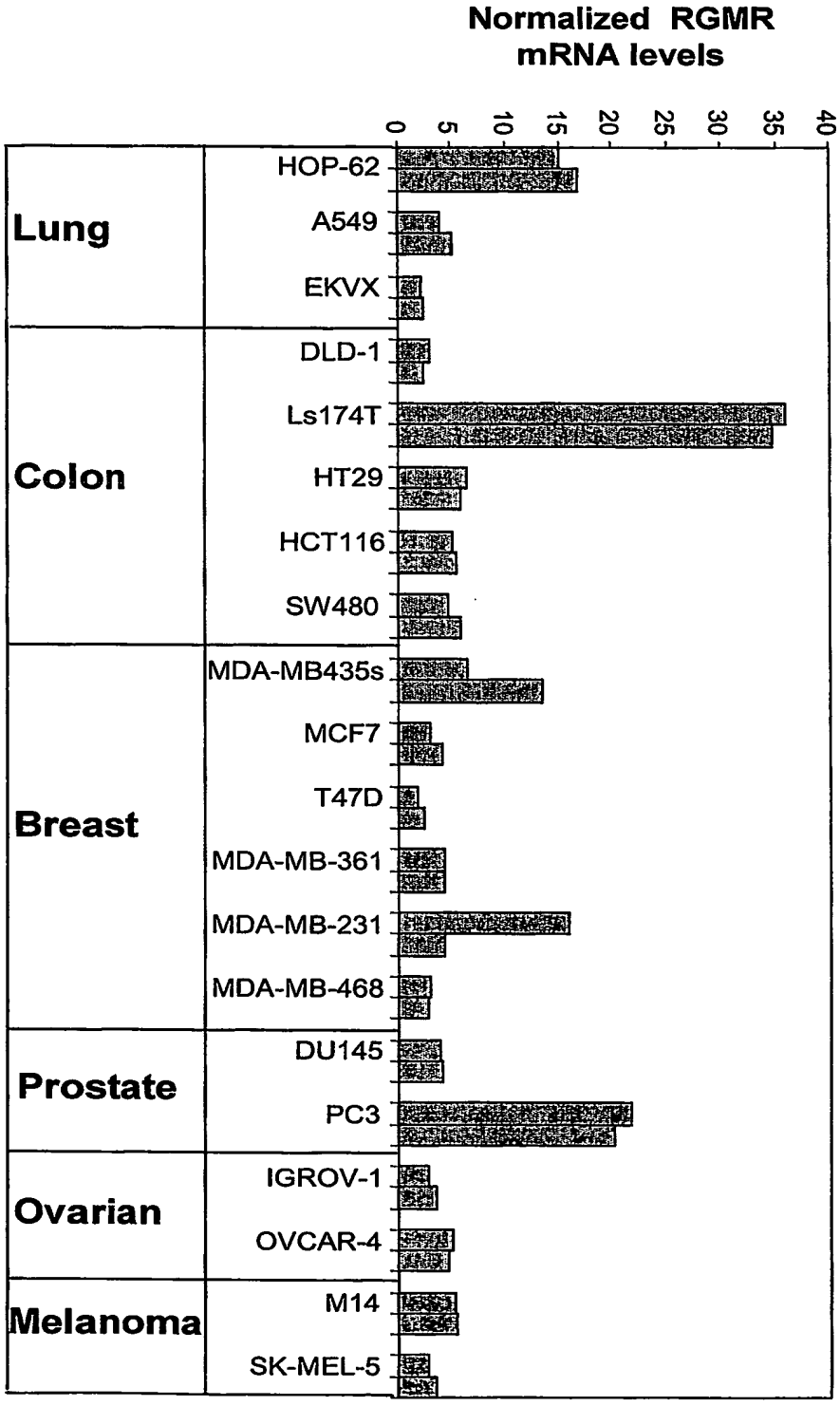

Normalized RGMR mRNA levels
0
5
10
15
20
25
30
35
40
Lung
HOP-62
A549
EKVX
Colon
DLD-1
Ls174T
HT29
HCT116
SW480
Breast
MDA-MB435s
MCF7
T47D
MDA-MB-361
MDA-MB-231
MDA-MB-468
Prostate
DU145
PC3
Ovarian
IGROV-1
OVCAR-4
Melanoma
M14
SK-MEL-5

FIG. 9C

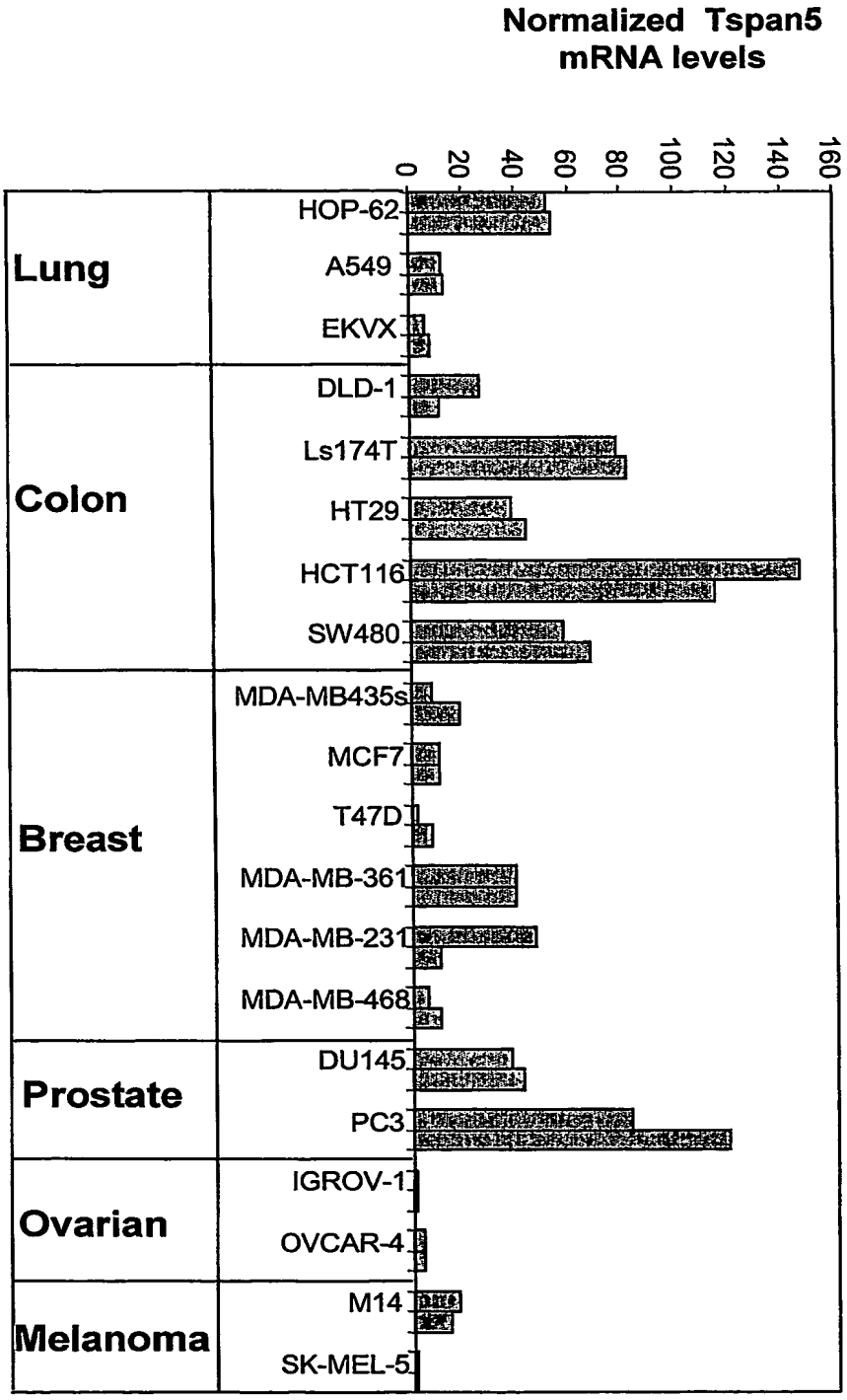

Normalized Tspan5 mRNA levels
0
20
40
60
80
100
120
140
160
Lung
HOP-62
A549
EKVX
Colon
DLD-1
Ls174T
HT29
HCT116
SW480
Breast
MDA-MB435s
MCF7
T47D
MDA-MB-361
MDA-MB-231
MDA-MB-468
Prostate
DU145
PC3
Ovarian
IGROV-1
OVCAR-4
Melanoma
M14
SK-MEL-5

FIG. 9D

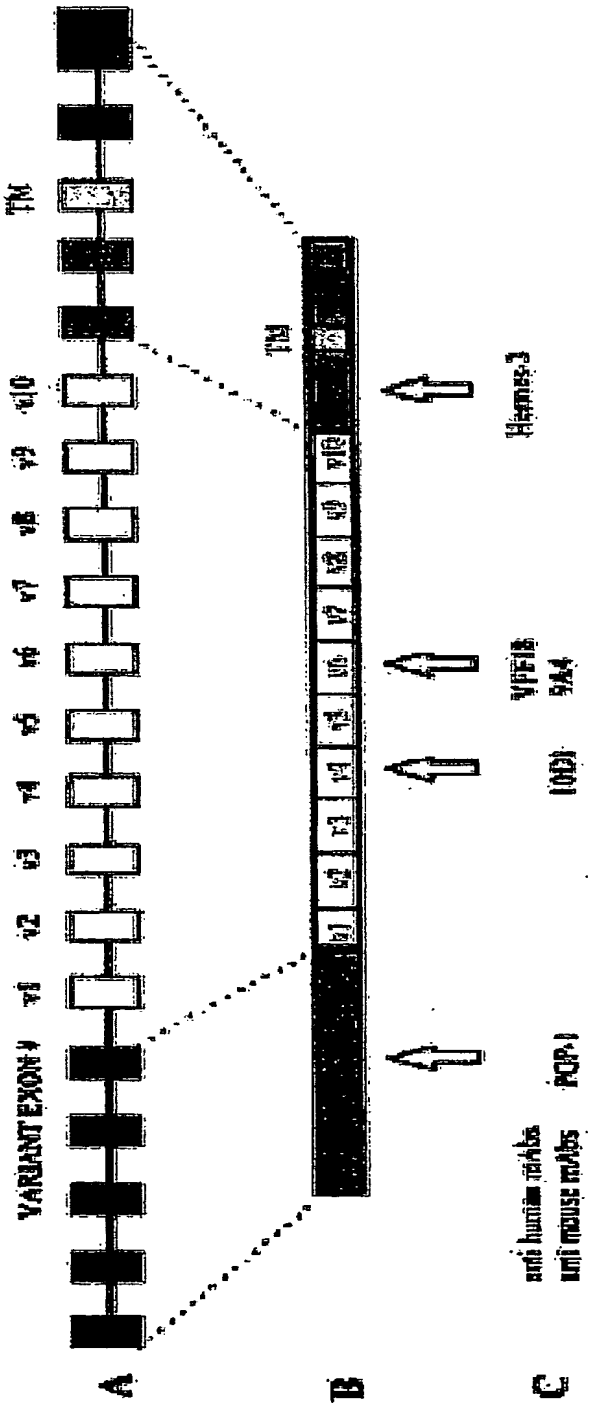

A
B
C
VARIANT EXON #
TM
anti human mAbs
anti mouse mAbs
(CD1)
Human 3

FIG. 10

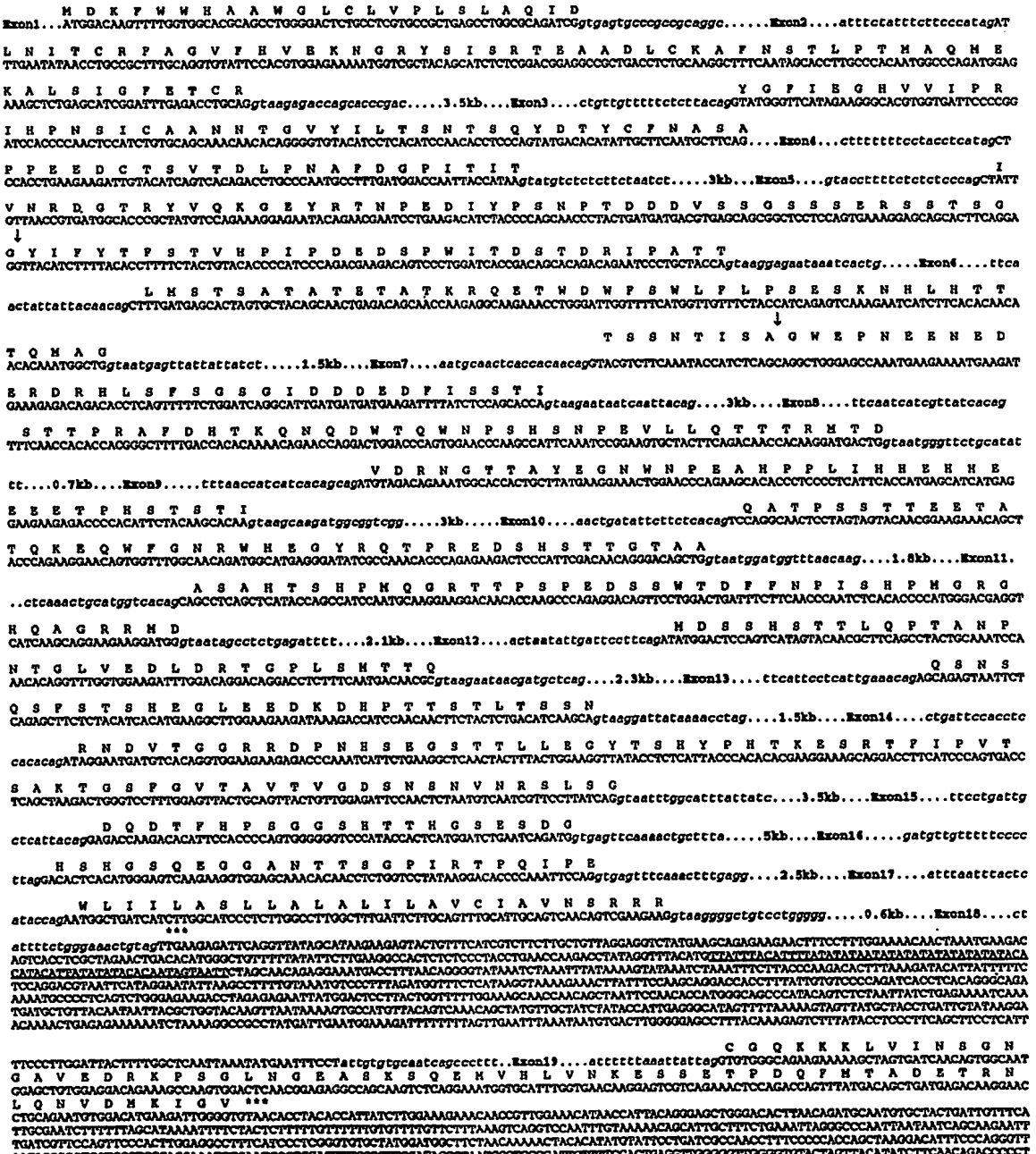


FIG. 11

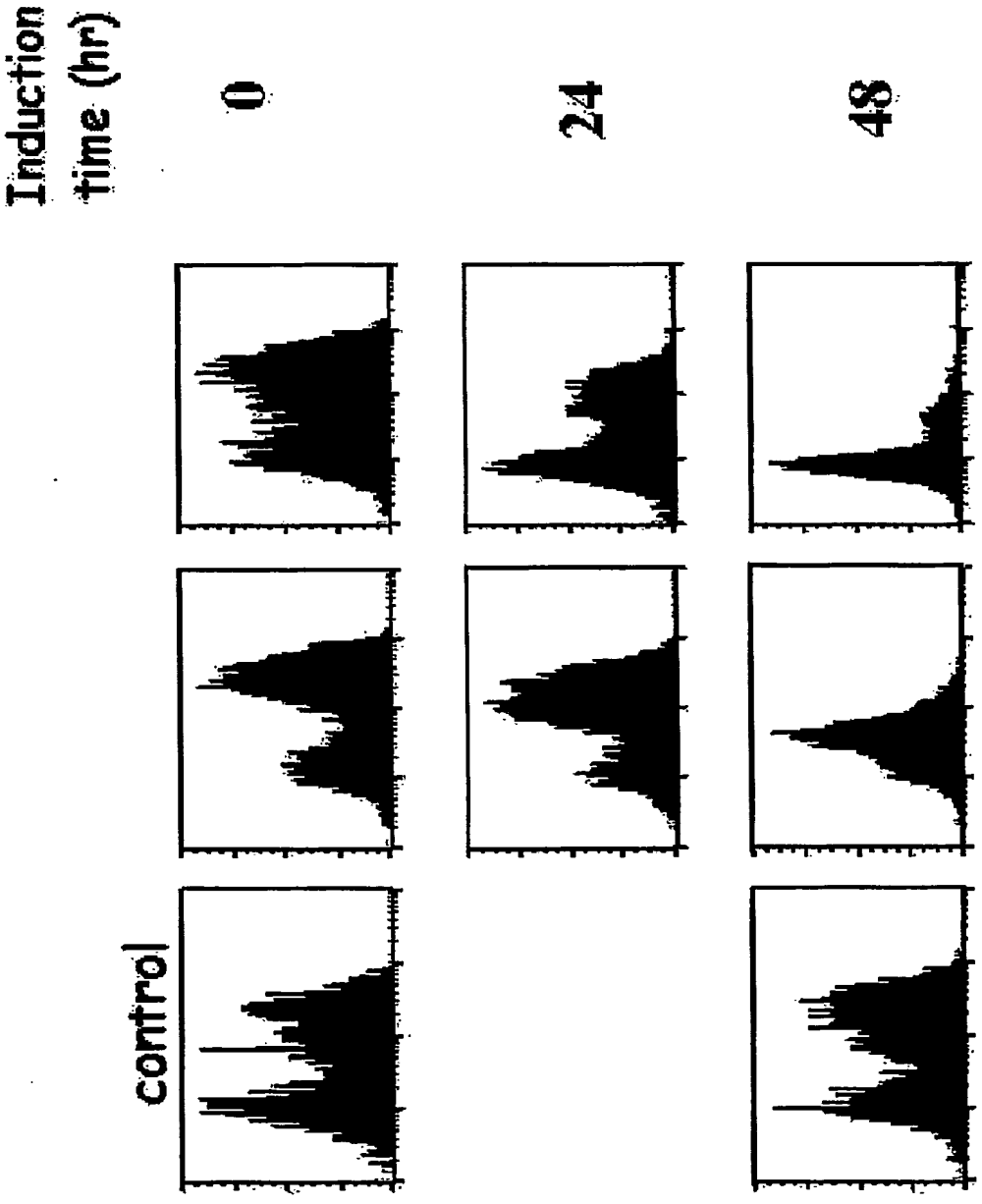


FIG. 12A

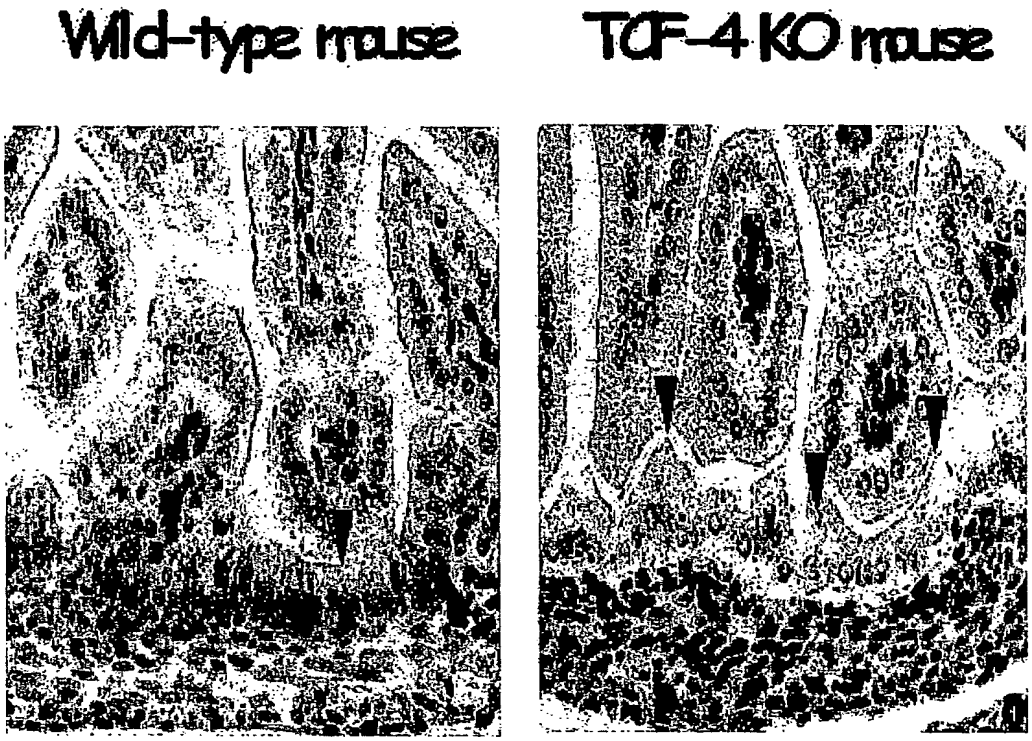


FIG. 12B

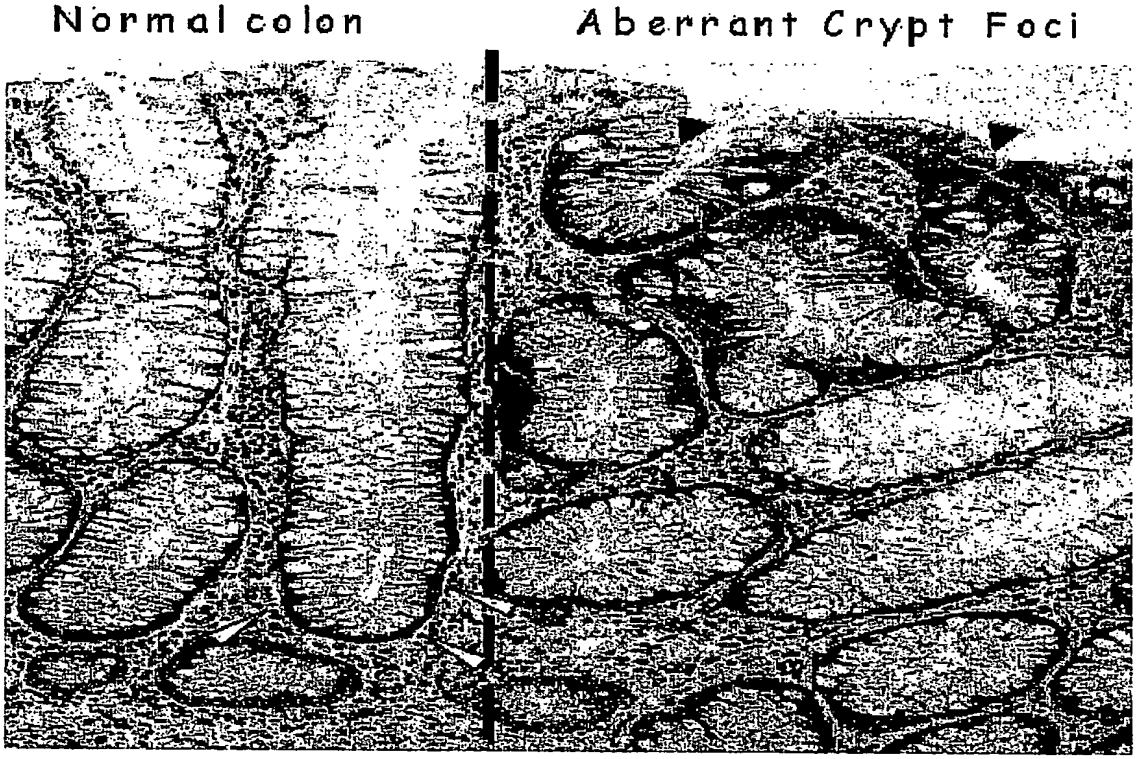


FIG. 13A

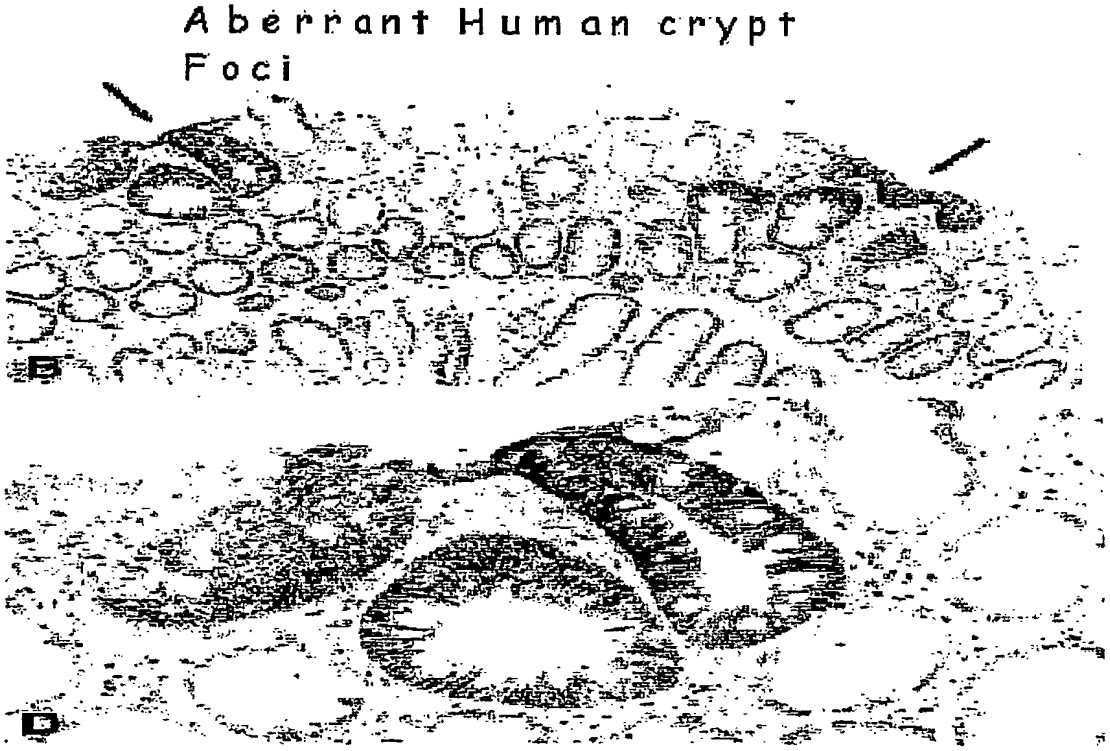


FIG. 13B

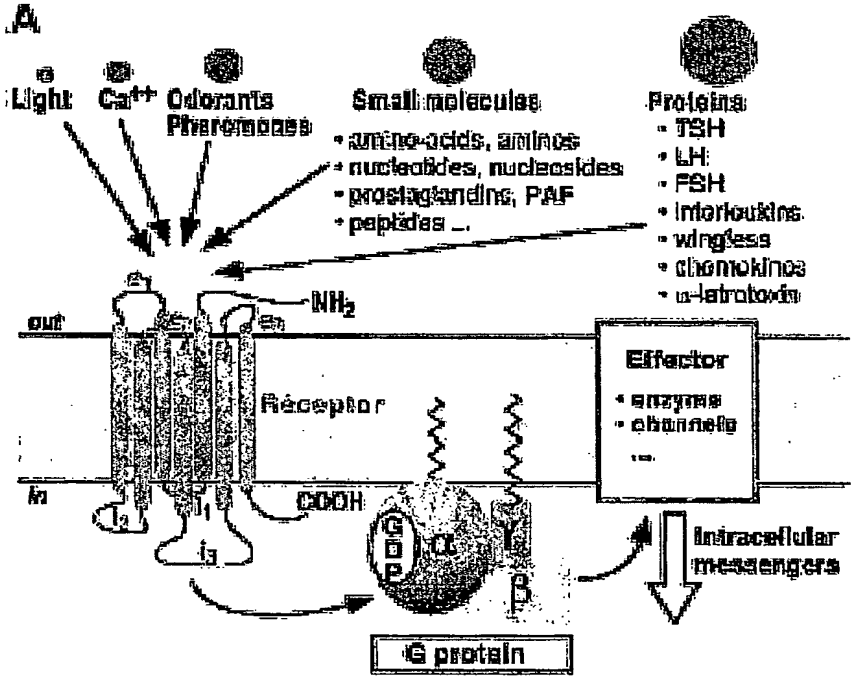

A
Light
Ca++
Odorants
Pheromones
Small molecules
• amino-acids, amines
• nucleotides, nucleosides
• prostaglandins, PAF
• peptides ...
Proteins
• TSH
• LH
• FSH
• interleukins
• wingless
• chemokines
• α-latrotoxin
NH2
out
in
Récepteur
COOH
Effector
• enzyme
• channels
...
Intracellular messengers
G protein

FIG. 14

Figure 1 : Lineup of RGM and RGMR Protein Sequences:

```
humanRGM        --MGRGAG--------------RSALGFWP------TLAFLLCSFPAATS-------PCK
mouseRGM        --MGRGAG--------------RSALGLWP------TLAFLLCSFPAAIS-------PCK
chickenRGM      --MGRGAG--------------STALGLFQ------ILPVFLCIFPPVTS-------PCK
XenopusRGM      MGMGRGAG--------------PKALGFFK------ILTVFLCTFHTVSS-------SCK
HumanRGMR       --MGLRAAPSSAAAAA-AEVEQRRRPGLCP--PPLELLLLLLFSLGLLHAGDCQQPAQCR
mouseRGMR       --MGVRAAPYCAAGPAGAGAEQSRRPRLWPPTPPPPLLLLLLLSLGLLHAGDCQQPTQCR
                  **  *.                    :         * .:*  :    :        *:

humanRGM        ILKCNSEFWSATS-GSHAPASDDTPEFCAALRSYALCTRRTARTCRGDLAYHSAVHGIED
mouseRGM        ILKCNSEFWSATSSGSHAPASDDVPEFCAALRTYALCTRRTARTCRGDLAYHSAVHGIED
chickenRGM      ILKCNSEFWAATS-GSHHLGAEETPEFCTALRAYAHCTRRTARTCRGDLAYHSAVHGIDD
XenopusRGM      ILKCTADYLQATSNPHHHTGAEDTVEICTALRTYAHCSRRTARTCRGDLAYHSTVHGIDD
HumanRGMR       IQKCTTDFVSLTSHLNSAVDGFDS-EFCKALRAYAGCTQRTSKACRGNLVYHSAVLGISD
mouseRGMR       IQKCTTDFVALTAHLNSAADGFDS-EFCKALRAYAGCTQRTSKACRGNLVYHSAVLGISD
                * **.:::   *:       . :  *:* ***:** *::**:::***:*.***:* **.*

humanRGM        LMSQHNCSKDGPTSQPRLRTLPPAGDSQERSDSPEICHYEKSFHKHSATPNYTHCGLFGD
mouseRGM        LMSQHNCSKDGPTSQPRVRTLPPAGDSQERSDSPEICHYEKSFHKHSAAPNYTHCGLFGD
chickenRGM      LMVQHNCSKDGPTSQPRLRTLPP-GDSQERSDSPEICHYEKSFHKHSAAPNYTHCGLFGD
XenopusRGM      LMSHHNCSKDGPTSQPRVRILPP-GDSQERSDSPEICHYEKSFHRPSALPNYTHCGLFGD
HumanRGMR       LMSQRNCSKDGPTSSTNPEVTHDPCNYHSHAGAREHRRGDQ------NPPSYLFCGLFGD
mouseRGMR       LMSQRNCSKDGPTSSTNPEVTHDPCNYHSHGGVREHGGGDQ------RPPNYLFCGLFGD
                ** ::*********... .      : :.:..  *    ::        *.* .******

humanRGM        PHLRTFTDRFQTCKVQGAWPLIDNNYLNVQATNTPVLPGSAATATSKLTIIFKNFQECVD
mouseRGM        PHLRTFTDHFQTCKVQGAWPLIDNNYLNVQVTNTPVLPGSAATATSKLTIIFKNFQECVD
chickenRGM      PHLRTFTDTFQTCKVQGAWPLIDNNYLNVQVTNTPVLPGSSATATSKLTIIFKSFQECVE
XenopusRGM      PHLRTFSDTFQTCKIQGAWPLIDNNYLNVQVTNTPVLPGSTATATSKLTIIFKNFQECVD
HumanRGMR       PHLRTFKDNFQTCKVEGAWPLIDNNYLSVQVTNVPVVPGSSATATNKITIIFKAHHECTD
mouseRGMR       PHLRTFKDHFQTCKVEGAWPLIDNNYLSVQVTNVPVVPGSSATATNKVTIIFKAQHECTD
                ******.* *****::***********.**.**.**:***:****.*:*****  :**.:
```

FIG. 15A

```
humanRGM        QKVYQAEMDELPAAFVDGSKNGGDKHGANSLKITEKVSGQHVEIQAKYIGTTIVVRQVGR
mouseRGM        QKVYQAEMDELPSAFADGSKNGGDKHGANSLKITEKVSGQHVEIQAKYIGTTIVVRQVGR
chickenRGM      QKVYQAEMDELPAAFADGSKNGGDKHGANSLKITEKVSGQHIEIQAKYIGTTIVVRQVGR
XenopusRGM      QKVYQAEMDELPAAFIDGSKNGGDKSGANSLRIIEKVSGQHIEIQAKYIGTTIVVRQVGH
HumanRGMR       QKVYQAVTDDLPAAFVDGTTSGGD-SDAKSLRIVERESGHYVEMHARYIGTTVFVRQVGR
mouseRGMR       QKVYQAVTDDLPAAFVDGTTSGGD-GDVKSLHIVEKESGRYVEMHARYIGTTVFVRQLGR
                ******  *:**:** **:..***  ..:**:* *: **:::*::*:*****:.***:*:

humanRGM        YLTFAVRMPEEVVNAVEDWDSQGLYLCLRGCPLNQQIDFQAFH-TNAEGTGARRLAAASP
mouseRGM        YLTFAVRMPEEVVNAVEDRDSQGLYLCLRGCPLNQQIDFQAFR-ANAE--SPRRPAAASP
chickenRGM      YLTFAVRMPEEVVNAVEDRDSQGLYLCLRGCPLNQQIDFQTFRLAQAAEGRARRKGPSLP
XenopusRGM      YLTFAVRMPEEVVNAVEDKDNQGLYLCLHGCPQNQQIDFRNFH-LQAPETGLKRLTSASS
HumanRGMR       YLTLAIRMPEDLAMSYEE--SQDLQLCVNGCPLSERIDDGQGQVSAILGHSLPRTSLVQA
mouseRGMR       YLTLAIRMPEDLAMSYEE--SQDLQLCVNGCPMSECIDDGQGQVSAILGHSLPHTTSVQA
                ***:*:****::. : *:  .*.* **:.*** .: **    :          :     .

humanRGM        APTAPETFPYETAVAKCKEKLPVEDLYYQACVFDLLTTGDVNFTLAAYYALEDVKMLHSN
mouseRGM        SPVVPETFPYETAVAKCKEKLPVEDLYYQACVFDLLTTGDVNFTLAAYYALEDGKMLHSN
chickenRGM      AP--PEAFTYESATAKCREKLPVEDLYFQSCVFDLLTTGDVNFMLAAYYAFEDVKMLHSN
XenopusRGM      AA----SFTPQTAEAKCKEKLPVKDLYFQSCVFDLLTTGDVNFTLAAYYAFEDVKLLHSN
HumanRGMR       WP----GYTLETANTQCHEKMPVKDIYFQSCVFDLLTTGDANFTAAAHSALEDVEALHPR
mouseRGMR       WP----GYTLETASTQCHEKMPVKDIYFQSCVFDLLTTGDANFTAAAHSALEDVEALHPR
                .     :. ::* ::*:**:**:*:*:*:**********.**  **: *:** : **..

humanRGM        KDKLHLYERTRDLPGRAAAG-----LPLAPRPLLGALVPLLALLPVFC---
mouseRGM        KDKLHLFERTRELPGAVAAAAAATTFPLAPQILLG-TIPLLVLLPVLW---
chickenRGM      KDKLHLYERTRALAPGNAAP------SEHPWALPALWVALLSLSQCWLGLL
XenopusRGM      KNKVHLFERP----------------------------------------
HumanRGMR       KERWHIFPSSGNGTP-----------RGGSDLSVSLGLTCLILIVFL----
mouseRGMR       KERWHIFPSSCG---------------GCRDLPVGLGLTCLILIMFL----
                *:: *::  .
```

FIG. 15B

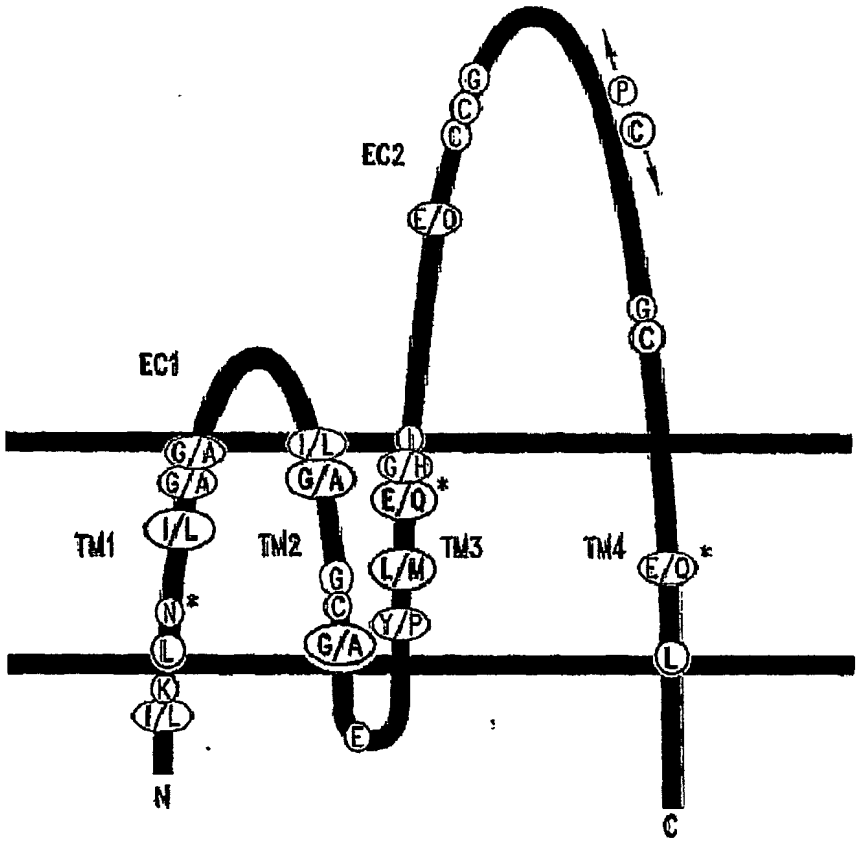


FIG. 16

ATGGACAAGTTTTGGTGGCACGCAGCCTGGGGACTCTGCCTCGTGCCGCTGAGCCTGGCGCAGATCGATTTGAATATAACCTGCCG
CTTTGCAGGTGTATTCCACGTGGAGAAAAATGGTCGCTACAGCATCTCTCGGACGGAGGCCGCTGACCTCTGCAAGGCTTTCAATA
GCACCTTGCCCACAATGGCCCAGATGGAGAAAGCTCTGAGCATCGGATTTGAGACCTGCAGGTATGGGTTCATAGAAGGGCACGTG
GTGATTCCCCGGATCCACCCCAACTCCATCTGTGCAGCAAACAACACAGGGGTGTACATCCTCACATCCAACACCTCCCAGTATGA
CACATATTGCTTCAATGCTTCAGCTCCACCTGAAGAAGATTGTACATCAGTCACAGACCTGCCCAATGCCTTTGATGGACCAATTA
CCATAACTATTGTTAACCGTGATGGCACCCGCTATGTCCAGAAAGGAGAATACAGAACGAATCCTGAAGACATCTACCCCAGCAAC
CCTACTGATGATGACGTGAGCAGCGGCTCCTCCAGTGAAAGGAGCAGCACTTCAGGAGGTTACATCTTTTACACCTTTTCTACTGT
ACACCCCATCCCAGACGAAGACAGTCCCTGGATCACCGACAGCACAGACAGAATCCCTGCTACCACTTTGATGAGCACTAGTGCTA
CAGCAACTGAGACAGCAACCAAGAGGCAAGAAACCTGGGATTGGTTTTCATGGTTGTTTCTACCATCAGAGTCAAAGAATCATCTT
CACACAACAACACAAATGGCTGGTACGTCTTCAAATACCATCTCAGCAGGCTGGGAGCCAAATGAAGAAAATGAAGATGAAAGAGA
CAGACACCTCAGTTTTTCTGGATCAGGCATTGATGATGATGAAGATTTTATCTCCAGCACCATTTCAACCACACCACGGGCTTTTG
ACCACACAAAACAGAACCAGGACTGGACCCAGTGGAACCCAAGCCATTCAAATCCGGAAGTGCTACTTCAGACAACCACAAGGATG
ACTGATGTAGACAGAAATGGCACCACTGCTTATGAAGGAAACTGGAACCCAGAAGCACACCCTCCCCTCATTCACCATGAGCATCA
TGAGGAAGAAGAGACCCCACATTCTACAAGCACAATCCAGGCAACTCCTAGTAGTACAACGGAAGAAACAGCTACCCAGAAGGAAC
AGTGGTTTGGCAACAGATGGCATGAGGGATATCGCCAAACACCCAGAGAAGACTCCCATTCGACAACAGGGACAGCTGCAGCCTCA
GCTCATACCAGCCATCCAATGCAAGGAAGGACAACACCAAGCCCAGAGGACAGTTCCTGGACTGATTTCTTCAACCCAATCTCACA
CCCCATGGGACGAGGTCATCAAGCAGGAAGAAGGATGGATATGGACTCCAGTCATAGTATAACGCTTCAGCCTACTGCAAATCCAA
ACACAGGTTTGGTGGAAGATTTGGACAGGACAGGACCTCTTTCAATGACAACGCAGCAGAGTAATTCTCAGAGCTTCTCTACATCA
CATGAAGGCTTGGAAGAAGATAAAGACCATCCAACAACTTCTACTCTGACATCAAGCAATAGGAATGATGTCACAGGTGGAAGAAG
AGACCCAAATCATTCTGAAGGCTCAACTACTTTACTGGAAGGTTATACCTCTCATTACCCACACACGAAGGAAAGCAGGACCTTCA
TCCCAGTGACCTCAGCTAAGACTGGGTCCTTTGGAGTTACTGCAGTTACTGTTGGAGATTCCAACTCTAATGTCAATCGTTCCTTA
TCAGGAGACCAAGACACATTCCACCCCAGTGGGGGGTCCCATACCACTCATGGATCTGAATCAGATGGACACTCACATGGGAGTCA
AGAAGGTGGAGCAAACACAACCTCTGGTCCTATAAGGACACCCCAAATTCCAGAATGGCTGATCATCTTGGCATCCCTCTTGGCCT
TGGCTTTGATTCTTGCAGTTTGCATTGCAGTCAACAGTCGAAGAAGGTGTGGGCAGAAGAAAAAGCTAGTGATCAACAGTGGCAAT
GGAGCTGTGGAGGACAGAAAGCCAAGTGGACTCAACGGAGAGGCCAGCAAGTCTCAGGAAATGGTGCATTTGGTGAACAAGGAGTC
GTCAGAAACTCCAGACCAGTTTATGACAGCTGATGAGACAAGGAACCTGCAGAATGTGGACATGAAGATTGGGGTGTAACACCTAC
ACCATTATCTTGGAAAGAAACAACCGTTGGAAACATAACCATTACAGGGAGCTGGGACACTTAACAGATGCAATGTGCTACTGATT
GTTTCATTGCGAATCTTTTTTAGCATAAAATTTTCTACTCTTTTTGTTTTTTTGTGTTTTGTTCTTTAAAGTCAGGTCCAATTTGTA
AAAACAGCATTGCTTTCTGAAATTAGGGCCCAATTAATAATCAGCAAGAATTTGATCGTTCCAGTTCCCACTTGGAGGCCTTTCAT
CCCTCGGGTGTGCTATGGATGGCTTCTAACAAAAACTACACATATGTATTCCTGATCGCCAACCTTTCCCCCACCAGCTAAGGACA
TTTCCCAGGGTTAATAGGGCCTGGTCCCTGGGAGGAAATTTGAATGGGTCCATTTTGCCCTTCCATAGCCTAATCCCTGGGCATTG
CTTTCCACTGAGGTTGGGGGTTGGGGTGTACTAGTTACACATCTTCAACAGACCCCCTCTAGAAATTTTTCAGATGCTTCTGGGAG
ACACCCAAAGGGTGAAGCTATTTATCTGTAGTAAACTATTTATCTGTGTTTTTGAAATATTAAACCCTGGATCAGTCCTTTGATCA
GTATAATTTTTTAAAGTTACTTTGTCAGAGGCACAAAAGGGTTTAAACTGATTCATAATAAATATCTGTACTTCTTCGATCTTCAC
CTTTTGTGCTGTGATTCTTCAGTTTCTAAACCAGCACTGTCTGGGTCCCTACAATGTATCAGGAAGAGCTGAGAATGGTAAGGAGA
CTCTTCTAAGTCTTCATCTCAGAGACCCTGAGTTCCCACTCAGACCCACTCAGCCAAATCTCATGGAAGACCAAGGAGGGCAGCAC
TGTTTTTGTTTTTTGTTTTTTGTTTTTTTTTTTTGACACTGTCCAAAGGTTTTCCATCCTGTCCTGGAATCAGAGTTGGAAGCTGA
GGAGCTTCAGCCTCTTTTATGGTTTAATGGCCACCTGTTCTCTCCTGTGAAAGGCTTTGCAAAGTCACATTAAGTTTGCATGACCT
GTTATCCCTGGGGCCCTATTTCATAGAGGCTGGCCCTATTAGTGATTTCCAAAAACAATATGGAAGTGCCTTTTGATGTCTTACAA
TAAGAGAAGAAGCCAATGGAAATGAAAGAGATTGGCAAAGGGGAAGGATGATGCCATGTAGATCCTGTTTGACATTTTTATGGCTG
TATTTGTAAACTTAAACACACCAGTGTCTGTTCTTGATGCAGTTGCTATTTAGGATGAGTTAAGTGCCTGGGGAGTCCCTCAAAGG
TTAAAGGGATTCCCATCATTGGAATCTTATCACCAGATAGGCAAGTTTATGACCAAACAAGAGAGTACTGGCTTTATCCTCTAACC
TCATATTTTCTCCCACTTGGCAAGTCCTTTGTGGCATTTATTCATCAGTCAGGGTGTCCGATTGGTCCTAGAACTTCCAAAGGCTG
CTTGTCATAGAAGCCATTGCATCTATAAAGCAACGGCTCCTGTTAAATGGTATCTCCTTTCTGAGGCTCCTACTAAAAGTCATTTG
TTACCTAAACTTATGTGCTTAACAGGCAATGCTTCTCAGACCACAAAGCAGAAAGAAGAAGAAAAGCTCCTGACTAAATCAGGGCT
GGGCTTAGACAGAGTTGATCTGTAGAATATCTTTAAAGGAGAGATGTCAACTTTCTGCACTATTCCCAGCCTCTGCTCCTCCCTGT
CTACCCTCTCCCCTCCCTCTCTCCCTCCACTTCACCCCACAATCTTGAAAAACTTCCTTTCTCTCTTCTGTGAACATCATTGGCCAGA
TCCATTTTCAGTGGTCTGGATTTCTTTTTATTTTCTTTTCAACTTGAAAGAAACTGGACATTAGGCCACTATGTGTTGTTACTGCC
ACTAGTGTTCAAGTGCCTCTTGTTTTCCCAGAGATTTCCTGGGTCTGCCAGAGGCCCAGACAGGCTCACTCAAGCTCTTTAACTGA
AAAGCAACAAGCCACTCCAGGACAAGGTTCAAAATGGTTACAACAGCCTCTACCTGTCGCCCCAGGGAGAAAGGGGTAGTGATACA
AGTCTCATAGCCAGAGATGGTTTTCCACTCCTTCTAGATATTCCCAAAAAGAGGCTGAGACAGGAGGTTATTTTCAATTTTATTTT
GGAATTAAATACTTTTTTCCCTTTATTACTGTTGTAGTCCCTCACTTGGATATACCTCTGTTTTCACGATAGAAATAAGGGAGGTC
TAGAGCTTCTATTCCTTGGCCATTGTCAACGGAGAGCTGGCCAAGTCTTCACAAACCCTTGCAACATTGCCTGAAGTTTATGGAAT
AAGATGTATTCTCACTCCCTTGATCTCAAGGGCGTAACTCTGGAAGCACAGCTTGACTACACGTCATTTTTACCAATGATTTTCAG
GTGACCTGGGCTAAGTCATTTAAACTGGGTCTTTATAAAAGTAAAAGGCCAACATTTAATTATTTTGCAAAGCAACCTAAGAGCTA
AAGATGTAATTTTTCTTGCAATTGTAAATCTTTTGTGTCTCCTGAAGACTTCCCTTAAAATTAGCTCTGAGTGAAAAATCAAAAGA
GACAAAAGACATCTTCGAATCCATATTTCAAGCCTGGTAGAATTGGCTTTTCTAGCAGAACCTTTCCAAAAGTTTTATATTGAGAT
TCATAACAACACCAAGAATTGATTTTGTAGCCAACATTCATTCAATACTGTTATATCAGAGGAGTAGGAGAGAGGAAACATTTGAC
TTATCTGGAAAAGCAAAATGTACTTAAGAATAAGAATAACATGGTCCATTCACCTTTATGTTATAGATATGTCTTTGTGTAAATCA
TTTGTTTTGAGTTTTCAAAGAATAGCCCATTGTTCATTCTTGTGCTGTACAATGACCACTGTTATTGTTACTTTGACTTTTCAGAG
CACACCCTTCCTCTGGTTTTTGTATATTTATTGATGGATCAATAATAATGAGGAAAGCATGATATGTATATTGCTGAGTTGAAAGC
ACTTATTGGAAAATATTAAAAGGCTAACATTAAAAGACTAAAGGAAACAGACTCAGA

(SEQ ID No. 1)

FIG. 17A

MDKFWWHAAWGLCLVPLSLAQIDLNITCRFAGVFHVEKNGRYSISRTEAADLCKAFNSTLPTMAQMEKALSIGFETCR
YGFIEGHVVIPRIHPNSICAANNTGVYILTSNTSQYDTYCFNASAPPEEDCTSVTDLPNAFDGPITITIVNRDGTRYVQKGE
YRTNPEDIYPSNPTDDDVSSGSSSERSSTSGGYIFYTFSTVHPIPDEDSPWITDSTDRIPATTLMSTSATATETATKRQETW
DWFSWLFLPSESKNHLHTTTQMAGTSSNTISAGWEPNEENEDERDRHLSFSGSGIDDDEDFISSTISTTPRAFDHTKQNQ
DWTQWNPSHSNPEVLLQTTTRMTDVDRNGTTAYEGNWNPEAHPPLIHHEHHEEEETPHSTSTIQATPSSTTEETATQKE
QWFGNRWHEGYRQTPREDSHSTTGTAAASAHTSHPMQGRTTPSPEDSSWTDFFNPISHPMGRGHQAGRRMDMDSSHSI
TLQPTANPNTGLVEDLDRTGPLSMTTQQSNSQSFSTSHEGLEEDKDHPTTSTLTSSNRNDVTGGRRDPNHSEGSTTLLEG
YTSHYPHTKESRTFIPVTSAKTGSFGVTAVTVGDSNSNVNRSLSGDQDTFHPSGGSHTTHGSESDGHSHGSQEGGANTT
SGPIRTPQIPEWLIILASLLALALILAVCIAVNSRRRCGQKKKLVINSGNGAVEDRKPSGLNGEASKSQEMVHLVNKESSE
TPDQFMTADETRNLQNVDMKIGV*

(SEQ ID No. 2)

FIG. 17B

ATGGACAAGTTTTGGTGGCACGCAGCCTGGGGACTCTGCCTCGTGCCGCTGAGCCTGGCGCAGATCGATTTGAATATAACCTGCCG
CTTTGCAGGTGTATTCCACGTGGAGAAAAATGGTCGCTACAGCATCTCTCGGACGGAGGCCGCTGACCTCTGCAAGGCTTTCAATA
GCACCTTGCCCACAATGGCCCAGATGGAGAAAGCTCTGAGCATCGGATTTGAGACCTGCAGGTATGGGTTCATAGAAGGGCATGTG
GTGATTCCCCGGATCCACCCCAACTCCATCTGTGCAGCAAACAACACAGGGGTGTACATCCTCACATACAACACCTCCCAGTATGA
CACATATTGCTTCAATGCTTCAGCTCCACCTGAAGAAGATTGTACATCAGTCACAGACCTGCCCAATGCCTTTGATGGACCAATTA
CCATAACTATTGTTAACCGTGATGGCACCCGCTATGTCCAGAAAGGAGAATACAGAACGAATCCTGAAGACATCTACCCCAGCAAC
CCTACTGATGATGACGTGAGCAGCGGCTCCTCCAGTGAAAGGAGCAGCACTTCAGGAGGTTACATCTTTTACACCTTTTCTACTGT
ACACCCCATCCCAGACGAAGACAGTCCCTGGATCACCGACAGCACAGACAGAATCCCTCGTACCAATATGGACTCCAGTCATAGTA
CAACGCTTCAGCCTACTGCAAATCCAAACACAGGTTTGGTGGAAGATTTGGACAGGACAGGACCTCTTTCAATGACAACGCAGCAG
AGTAATTCTCAGAGCTTCTCTACATCACATGAAGGCTTGGAAGAAGATAAAGACCATCCAACAACTTCTACTCTGACATCAAGCAA
TAGGAATGATGTCACAGGTGGAAGAAGAGACCCAAATCATTCTGAAGGCTCAACTCATTTACTGGAAGGTTATACCTCTCATTACC
CACACACGAAGGAAAGCAGGACCTTCATCCCAGTGACCTCAGCTAAGACTGGGTCCTTTGGAGTTACTGCAGTTACTGTTGGAGAT
TCCAACTCTAATGTCAATCGTTCCTTATCAGGAGACCAAGACACATTCCACCCCAGTGGGGGGTCCCATACCACTCATGGATCTGA
ATCAGATGGACACTCACATGGGAGTCAAGAAGGTGGAGCAAACACAACCTCTGGTCCTATAAGGACACCCCAAATTCCAGAATGGC
TGATCATCTTGGCATCCCTCTTGGCCTTGGCTTTGATTCTTGCAGTTTGCATTGCAGTCAACAGTCGAAGAAGGTGTGGGCAGAAG
AAAAAGCTAGTGATCAACAGTGGCAATGGAGCTGTGGAGGACAGAAAGCCAAGTGGACTCAACGGAGAGGCCAGCAAGTCTCAGGA
AATGGTGCATTTGGTGAACAAGGAGTCGTCAGAAACTCCAGACCAGTTTATGACAGCTGATGAGACAAGGAACCTGCAGAATGTGG
ACATGAAGATTGGGGTGTAA

FIG. 18A

MDKFWWHAAWGLCLVPLSLAQIDLNITCRFAGVFHVEKNGRYSISRTEAADLCKAFNSTLPTMAQMEKALSIGFETCRYGFIEGHV
VIPRIHPNSICAANNTGVYILTYNTSQYDTYCFNASAPPEEDCTSVTDLPNAFDGPITITIVNRDGTRYVQKGEYRTNPEDIYPSN
PTDDDVSSGSSSERSSTSGGYIFYTFSTVHPIPDEDSPWITDSTDRIPRTNMDSSHSTTLQPTANPNTGLVEDLDRTGPLSMTTQQ
SNSQSFSTSHEGLEEDKDHPTTSTLTSSNRNDVTGGRRDPNHSEGSTHLLEGYTSHYPHTKESRTFIPVTSAKTGSFGVTAVTVGD
SNSNVNRSLSGDQDTFHPSGGSHTTHGSESDGHSHGSQEGGANTTSGPIRTPQIPEWLIILASLLALALILAVCIAVNSRRRCGQK
KKLVINSGNGAVEDRKPSGLNGEASKSQEMVHLVNKESSETPDQFMTADETRNLQNVDMKIGV

FIG. 18B

CTTTGATGAGCACTAGTGCTACAGCAACTGAGACAGCAACCAAGAGGCAAGAAGCCTGGGATTGGTTTTCATGGTTGTTTCTACCA
TCAGAGTCAAAGAATCATCTTCACACAACAACACAAATGGCTG

FIG. 19A

GTACGTCTTCAAATACCATCTCAGCAGGCTGGGAGCCAAATGAAGAAAATGAAGATGAAAGAGACAGACACCTCAGTTTTTCTGGA
TCAGGCATTGATGATGATGAAGATTTTATCTCCAGCACCA

FIG. 19B

TTTCAACCACACCACGGGCCTTTGACCACACAAAACAGAACCAGGACTGGACCCAGTGGAACCCAAGCCATTCAAATCCGGAAGTG
CTACTTCAGACAACCACAAGGATGACTG

FIG. 19C

ATGTAGACAGAAATGGCACCACTGCTTATGAAGGAAACTGGAACCCAGAAGCACACCCTCCCCTCATTCACCATGAGCATCATGAG
GAAGAAGAGACCCCACATTCTACAAGCACAA

FIG. 19D

TCCAGGCAACTCCTAGTAGTACAACGGAAGAAACAGCTACCCAGAAGGAACAGTGGTTTGGCAACAGATGGCATGAGGGATATCGC
CAAACACCCAGAGAAGACTCCCATTCGACAACAGGGACAGCTG

FIG. 19E

CAGCCTCAGCTCATACCAGCCATCCAATGCAAGGAAGGACAACACCAAGCCCAGAGGACAGTTCCTGGACTGATTTCTTCAACCCA
ATCTCACACCCCATGGGACGAGGTCATCAAGCAGGAAGAAGGATGG

FIG. 19F

ATATGGACTCCAGTCATAGTACAACGCTTCAGCCTACTGCAAATCCAAACACAGGTTTGGTGGAAAATTTGGACAGGACAGGACCT
CTTTCAATGACAACGC

FIG. 19G

AGCAGAGTAATTCTCAGAGCTTCTCTACATCACATGAAGGCTTGGAAGAAGATAAAGACCATCCAACAACTTCTACTCTGACATCA
AGCA

FIG. 19H

ATAGGAATGATGTCACAGGTGGAAGAAGAGACCCAAATCATTCTGAAGGCTCAACTACTTTACTGGAAGGTTATACCTCTCATTAC
CCACACACGAAGGAAAGCAGGACCTTCATCCCAGTGACCTCAGCTAAGACTGGGTCCTTTGGAGTTACTGCAGTTACTGTTGGAGA
TTCCAACTCTAATGTCAATCGTTCCTTATCAG

FIG. 19I

Sequences of GPR49

A) Nucleic sequence GPR49 mRNA sequence:

>gi|4504378|ref|NM_003667.1| Homo sapiens G protein-coupled receptor 49 (GPR49), mRNA

ATGGACACCTCCCGGCTCGGTGTGCTCCTGTCCTTGCCTGTGCTGCTGCAGCTGGCGACCGGGGGCAGCTC
TCCCAGGTCTGGTGTGTTGCTGAGGGGCTGCCCCACACACTGTCATTGCGAGCCCGACGGCAGGATGTTGC
TCAGGGTGGACTGCTCCGACCTGGGGCTCTCGGAGCTGCCTTCCAACCTCAGCGTCTTCACCTCCTACCTA
GACCTCAGTATGAACAACATCAGTCAGCTGCTCCCGAATCCCCTGCCCAGTCTCCGCTTCCTGGAGGAGTT
ACGTCTTGCGGGAAACGCTCTGACATACATTCCCAAGGGAGCATTCACTGGCCTTTACAGTCTTAAAGTTC
TTATGCTGCAGAATAATCAGCTAAGACACGTACCCACAGAAGCTCTGCAGAATTTGCGAAGCCTTCAATCC
CTGCGTCTGGATGCTAACCACATCAGCTATGTGCCCCCAAGCTGTTTCAGTGGCCTGCATTCCCTGAGGCA
CCTGTGGCTGGATGACAATGCGTTAACAGAAATCCCCGTCCAGGCTTTTAGAAGTTTATCGGCATTGCAAG
CCATGACCTTGGCCCTGAACAAAATACACCACATACCAGACTATGCCTTTGGAAACCTCTCCAGCTTGGTA
GTTCTACATCTCCATAACAATAGAATCCACTCCCTGGGAAAGAAATGCTTTGATGGGCTCCACAGCCTAGA
GACTTTAGATTTAAATTACAATAACCTTGATGAATTCCCCACTGCAATTAGGACACTCTCCAACCTTAAAG
AACTAGGATTTCATAGCAACAATATCAGGTCGATACCTGAGAAAGCATTTGTAGGCAACCCTTCTCTTATT
ACAATACATTTCTATGACAATCCCATCCAATTTGTTGGGAGATCTGCTTTTCAACATTTACCTGAACTAAG
AACACTGACTCTGAATGGTGCCTCACAAATAACTGAATTTCCTGATTTAACTGGAACTGCAAACCTGGAGA
GTCTGACTTTAACTGGAGCACAGATCTCATCTCTTCCTCAAACCGTCTGCAATCAGTTACCTAATCTCCAA
GTGCTAGATCTGTCTTACAACCTATTAGAAGATTTACCCAGTTTTTCAGTCTGCCAAAAGCTTCAGAAAAT
TGACCTAAGACATAATGAAATCTACGAAATTAAAGTTGACACTTTCCAGCAGTTGCTTAGCCTCCGATCGC
TGAATTTGGCTTGGAACAAAATTGCTATTATTCACCCCAATGCATTTTCCACTTTGCCATCCCTAATAAAG
CTGGACCTATCGTCCAACCTCCTGTCGTCTTTTCCTATAACTGGGTTACATGGTTTAACTCACTTAAAATT
AACAGGAAATCATGCCTTACAGAGCTTGATATCATCTGAAAACTTTCCAGAACTCAAGGTTATAGAAATGC
CTTATGCTTACCAGTGCTGTGCATTTGGAGTGTGTGAGAATGCCTATAAGATTTCTAATCAATGGAATAAA
GGTGACAACAGCAGTATGGACGACCTTCATAAGAAAGATGCTGGAATGTTTCAGGCTCAAGATGAACGTGA
CCTTGAAGATTTCCTGCTTGACTTTGAGGAAGACCTGAAAGCCCTTCATTCAGTGCAGTGTTCACCTTCCC
CAGGCCCCTTCAAACCCTGTGAACACCTGCTTGATGGCTGGCTGATCAGAATTGGAGTGTGGACCATAGCA
GTTCTGGCACTTACTTGTAATGCTTTGGTGACTTCAACAGTTTTCAGATCCCCTCTGTACATTTCCCCCAT
TAAACTGTTAATTGGGGTCATCGCAGCAGTGAACATGCTCACGGGAGTCTCCAGTGCCGTGCTGGCTGGTG
TGGATGCGTTCACTTTTGGCAGCTTTGCACGACATGGTGCCTGGTGGGAGAATGGGGTTGGTTGCCATGTC
ATTGGTTTTTTGTCCATTTTTGCTTCAGAATCATCTGTTTTCCTGCTTACTCTGGCAGCCCTGGAGCGTGG
GTTCTCTGTGAAATATTCTGCAAAATTTGAAACGAAAGCTCCATTTTCTAGCCTGAAAGTAATCATTTTGC
TCTGTGCCCTGCTGGCCTTGACCATGGCCGCAGTTCCCCTGCTGGGTGGCAGCAAGTATGGCGCCTCCCCT
CTCTGCCTGCCTTTGCCTTTTGGGGAGCCCAGCACCATGGGCTACATGGTCGCTCTCATCTTGCTCAATTC
CCTTTGCTTCCTCATGATGACCATTGCCTACACCAAGCTCTACTGCAATTTGGACAAGGGAGACCTGGAGA
ATATTTGGGACTGCTCTATGGTAAAACACATTGCCCTGTTGCTCTTCACCAACTGCATCCTAAACTGCCCT
GTGGCTTTCTTGTCCTTCTCCTCTTTAATAAACCTTACATTTATCAGTCCTGAAGTAATTAAGTTTATCCT
TCTGGTGGTAGTCCCACTTCCTGCATGTCTCAATCCCCTTCTCTACATCTTGTTCAATCCTCACTTTAAGG
AGGATCTGGTGAGCCTGAGAAAGCAAACCTACGTCTGGACAAGATCAAAACACCCAAGCTTGATGTCAATT
AACTCTGATGATGTCGAAAAACAGTCCTGTGACTCAACTCAAGCCTTGGTAACCTTTACCAGCTCCAGCAT
CACTTATGACCTGCCTCCCAGTTCCGTGCCATCACCAGCTTATCCAGTGACTGAGAGCTGCCATCTTTCCT
CTGTGGCATTTGTCCCATGTCTCTAA (SEQ ID No.3)

FIG. 20A

B) Proteic sequence

>gi|4504379|ref|NP_003658.1| (NM_003667) G protein-coupled receptor 49; G protein-coupled receptor 67; orphan G protein-coupled receptor HG38 [Homo sapiens]

MDTSRLGVLLSLPVLLQLATGGSSPRSGVLLRGCPTHCHCEPDGRMLLRVDCSDLGLSELPSNLSVFTS
YLDLSMNNISQLLPNPLPSLRFLEELRLAGNALTYIPKGAFTGLYSLKVLMLQNNQLRHVPTEALQNLR
SLQSLRLDANHISYVPPSCFSGLHSLRHLWLDDNALTEIPVQAFRSLSALQAMTLALNKIHHIPDYAFG
NLSSLVVLHLHNNRIHSLGKKCFDGLHSLETLDLNYNNLDEFPTAIRTLSNLKELGFHSNNIRSIPEKA
FVGNPSLITIHFYDNPIQFVGRSAFQHLPELRTLTLNGASQITEFPDLTGTANLESLTLTGAQISSLPQ
TVCNQLPNLQVLDLSYNLLEDLPSFSVCQKLQKIDLRHNEIYEIKVDTFQQLLSLRSLNLAWNKIAIIH
PNAFSTLPSLIKLDLSSNLLSSFPITGLHGLTHLKLTGNHALQSLISSENFPELKVIEMPYAYQCCAFG
VCENAYKISNQWNKGDNSSMDDLHKKDAGMFQAQDERDLEDFLLDFEEDLKALHSVQCSPSPGPFKPCE
HLLDGWLIRIGVWTIAVLALTCNALVTSTVFRSPLYISPIKLLIGVIAAVNMLTGVSSAVLAGVDAFTF
GSFARHGAWWENGVGCHVIGFLSIFASESSVFLLTLAALERGFSVKYSAKFETKAPFSSLKVIILLCAL
LALTMAAVPLLGGSKYGASPLCLPLPFGEPSTMGYMVALILLNSLCFLMMTIAYTKLYCNLDKGDLENI
WDCSMVKHIALLLFTNCILNCPVAFLSFSSLINLTFISPEVIKFILLVVVPLPACLNPLLYILFNPHFK
EDLVSLRKQTYVWTRSKHPSLMSINSDDVEKQSCDSTQALVTFTSSSITYDLPPSSVPSPAYPVTESCH
LSSVAFVPCL (SEQ ID No.4)

FIG. 20B

EPHB4 sequence:

A) Nucleic sequence

>gi|17975769|ref|NM_004444.2| Homo sapiens EphB4 (EPHB4), mRNA

CGTCCACCCGCCCAGGGAGAGTCAGACCTGGGGGGGCGAGGGCCCCCCAAACTCAGT
TCGGATCCTACCCGAGTGAGGCGGCGCCATGGAGCTCCGGGTGCTGCTCTGCTGGGC
TTCGTTGGCCGCAGCTTTGGAAGAGACCCTGCTGAACACAAAATTGGAAACTGCTGA
TCTGAAGTGGGTGACATTCCCTCAGGTGGACGGGCAGTGGGAGGAACTGAGCGGCCT
GGATGAGGAACAGCACAGCGTGCGCACCTACGAAGTGTGTGAAGTGCAGCGTGCCCC
GGGCCAGGCCCACTGGCTTCGCACAGGTTGGGTCCCACGGCGGGGCGCCGTCCACGT
GTACGCCACGCTGCGCTTCACCATGCTCGAGTGCCTGTCCCTGCCTCGGGCTGGGCG
CTCCTGCAAGGAGACCTTCACCGTCTTCTACTATGAGAGCGATGCGGACACGGCCAC
GGCCCTCACGCCAGCCTGGATGGAGAACCCCTACATCAAGGTGGACACGGTGGCCGC
GGAGCATCTCACCCGGAAGCGCCCTGGGGCCGAGGCCACCGGGAAGGTGAATGTCAA
GACGCTGCGTCTGGGACCGCTCAGCAAGGCTGGCTTCTACCTGGCCTTCCAGGACCA
GGGTGCCTGCATGGCCCTGCTATCCCTGCACCTCTTCTACAAAAAGTGCGCCCAGCT
GACTGTGAACCTGACTCGATTCCCGGAGACTGTGCCTCGGGAGCTGGTTGTGCCCGT
GGCCGGTAGCTGCGTGGTGGATGCCGTCCCCGCCCCTGGCCCCAGCCCCAGCCTCTA
CTGCCGTGAGGATGGCCAGTGGGCCGAACAGCCGGTCACGGGCTGCAGCTGTGCTCC
GGGGTTCGAGGCAGCTGAGGGGAACACCAAGTGCCGAGCCTGTGCCCAGGGCACCTT
CAAGCCCCTGTCAGGAGAAGGGTCCTGCCAGCCATGCCCAGCCAATAGCCACTCTAA
CACCATTGGATCAGCCGTCTGCCAGTGCCGCGTCGGGTACTTCCGGGCACGCACAGA
CCCCCGGGGTGCACCCTGCACCACCCCTCCTTCGGCTCCGCGGAGCGTGGTTTCCCG
CCTGAACGGCTCCTCCCTGCACCTGGAATGGAGTGCCCCCCTGGAGTCTGGTGGCCG
AGAGGACCTCACCTACGCCCTCCGCTGCCGGGAGTGCCGACCCGGAGGCTCCTGTGC
GCCCTGCGGGGGAGACCTGACTTTTGACCCCGGCCCCCGGGACCTGGTGGAGCCCTG
GGTGGTGGTTCGAGGGCTACGTCCGGACTTCACCTATACCTTTGAGGTCACTGCATT
GAACGGGGTATCCTCCTTAGCCACGGGGCCCGTCCCATTTGAGCCTGTCAATGTCAC
CACTGACCGAGAGGTACCTCCTGCAGTGTCTGACATCCGGGTGACGCGGTCCTCACC
CAGCAGCTTGAGCCTGGCCTGGGCTGTTCCCCGGGCACCCAGTGGGGCGTGGCTGGA
CTACGAGGTCAAATACCATGAGAAGGGCGCCGAGGGTCCCAGCAGCGTGCGGTTCCT
GAAGACGTCAGAAAACCGGGCAGAGCTGCGGGGGCTGAAGCGGGGAGCCAGCTACCT
GGTGCAGGTACGGGCGCGCTCTGAGGCCGGCTACGGGCCCTTCGGCCAGGAACATCA
CAGCCAGACCCAACTGGATGAGAGCGAGGGCTGGCGGGAGCAGCTGGCCCTGATTGC
GGGCACGGCAGTCGTGGGTGTGGTCCTGGTCCTGGTGGTCATTGTGGTCGCAGTTCT
CTGCCTCAGGAAGCAGAGCAATGGGAGAGAAGCAGAATATTCGGACAAACACGGACA
GTATCTCATCGGACATGGTACTAAGGTCTACATCGACCCCTTCACTTATGAAGACCC
TAATGAGGCTGTGAGGGAATTTGCAAAAGAGATCGATGTCTCCTACGTCAAGATTGA
AGAGGTGATTGGTGCAGGTGAGTTTGGCGAGGTGTGCCGGGGGCGGCTCAAGGCCCC
AGGGAAGAAGGAGAGCTGTGTGGCAATCAAGACCCTGAAGGGTGGCTACACGGAGCG
GCAGCGGCGTGAGTTTCTGAGCGAGGCCTCCATCATGGGCCAGTTCGAGCACCCCAA
TATCATCCGCCTGGAGGGCGTGGTCACCAACAGCATGCCCGTCATGATTCTCACAGA
GTTCATGGAGAACGGCGCCCTGGACTCCTTCCTGCGGCTAAACGACGGACAGTTCAC
AGTCATCCAGCTCGTGGGCATGCTGCGGGGCATCGCCTCGGGCATGCGGTACCTTGC
CGAGATGAGCTACGTCCACCGAGACCTGGCTGCTCGCAACATCCTAGTCAACAGCAA

FIG. 21A

CCTCGTCTGCAAAGTGTCTGACTTTGGCCTTTCCCGATTCCTGGAGGAGAACTCTTC
CGATCCCACCTACACGAGCTCCCTGGGAGGAAAGATTCCCATCCGATGGACTGCCCC
GGAGGCCATTGCCTTCCGGAAGTTCACTTCCGCCAGTGATGCCTGGAGTTACGGGAT
TGTGATGTGGGAGGTGATGTCATTTGGGGAGAGGCCGTACTGGGACATGAGCAATCA
GGACGTGATCAATGCCATTGAACAGGACTACCGGCTGCCCCCGCCCCCAGACTGTCC
CACCTCCCTCCACCAGCTCATGCTGGACTGTTGGCAGAAAGACCGGAATGCCCGGCC
CCGCTTCCCCCAGGTGGTCAGCGCCCTGGACAAGATGATCCGGAACCCCGCCAGCCT
CAAAATCGTGGCCCGGGAGAATGGCGGGGCCTCACACCCTCTCCTGGACCAGCGGCA
GCCTCACTACTCAGCTTTTGGCTCTGTGGGCGAGTGGCTTCGGGCCATCAAAATGGG
AAGATACGAAGAAAGTTTCGCAGCCGCTGGCTTTGGCTCCTTCGAGCTGGTCAGCCA
GATCTCTGCTGAGGACCTGCTCCGAATCGGAGTCACTCTGGCGGGACACCAGAAGAA
AATCTTGGCCAGTGTCCAGCACATGAAGTCCCAGGCCAAGCCGGGACCCCGGGTGGG
ACAGGAGGACCGGCCCCGCAGTACTGACCTGCAGGAACTCCCCACCCCAGGGACACC
GCCTCCCCATTTTCCGGGGCAGAGTGGGGACTCACAGAGGCCCCCAGCCCTGTGCCC
CGCTGGATTGCACTTTGAGCCCGTGGGGTGAGGAGTTGGCAATTTGGAGAGACAGGA
TTTGGGGGTTCTGCCATAATAGGAGGGGAAAATCACCCCCCAGCCACCTCGGGGAAC
TCCAGACCAAGGGTGAGGGCGCCTTTCCCTCAGGACTGGGTGTGACCAGAGGAAAAG
GAAGTGCCCAACATCTCCCAGCCTCCCCAGGTGCCCCCCTCACCTTGATGGGTGCGT
TCCCGCAGACCAAAGAGAGTGTGACTCCCTTGCCAGCTCCAGAGTGGGGGGGCTGTC
CCAGGGGGCAAGAAGGGGTGTCAGGGCCCAGTGACAAAATCATTGGGGTTTGTAGTC
CCAACTTGCTGCTGTCACCACCAAACTCAATCATTTTTTTCCCTTGTAAATGCCCCT
CCCCCAGCTGCTGCCTTCATATTGAAGGTTTTTGAGTTTTGTTTTTGGTCTTAATTT
TTCTCCCCGTTCCCTTTTTGTTTCTTCGTTTTGTTTTTCTACCGTCCTTGTCATAAC
TTTGTGTTGGAGGGAACCTGTTTCACTATGGCCTCCTTTGCCCAAGTTGAAACAGGG
GCCCATCATCATGTCTGTTTCCAGAACAGTGCCTTGGTCATCCCACATCCCCGGACC
CCGCCTGGGACCCCCAAGCTGTGTCCTATGAAGGGGTGTGGGGTGAGGTAGTGAAAA
GGGCGGTAGTTGGTGGTGGAACCCAGAAACGGACGCCGGTGCTTGGAGGGGTTCTTA
AATTATATTTAAAAAAGTAACTTTTTGTATAAATAAAAGAAAATGGGACGTGTCCCA
GCTCCAGGGGT (SEQ ID No.5)

FIG. 21B

B) Proteic sequence

>gi|17975770|ref|NP_004435.2| (NM_004444) ephrin receptor EphB4 precursor. Ephrin receptor EphB4 (hepatoma transmembrane kinase); Tyro11; ephrin receptor EphB4; hepatoma transmembrane kinase [Homo sapiens]

MELRVLLCWASLAAALEETLLNTKLETADLKWVTFPQVDGQWEELSGLDEEQHSVRTYEVCEVQRAPGQAH
WLRTGWVPRRGAVHVYATLRFTMLECLSLPRAGRSCKETFTVFYYESDADTATALTPAWMENPYIKVDTVA
AEHLTRKRPGAEATGKVNVKTLRLGPLSKAGFYLAFQDQGACMALLSLHLFYKKCAQLTVNLTRFPETVPR
ELVVPVAGSCVVDAVPAPGPSPSLYCREDGQWAEQPVTGCSCAPGFEAAEGNTKCRACAQGTFKPLSGEGS
CQPCPANSHSNTIGSAVCQCRVGYFRARTDPRGAPCTTPPSAPRSVVSRLNGSSLHLEWSAPLESGGREDL
TYALRCRECRPGGSCAPCGGDLTFDPGPRDLVEPWVVVRGLRPDFTYTFEVTALNGVSSLATGPVPFEPVN
VTTDREVPPAVSDIRVTRSSPSSLSLAWAVPRAPSGAWLDYEVKYHEKGAEGPSSVRFLKTSENRAELRGL
KRGASYLVQVRARSEAGYGPFGQEHHSQTQLDESEGWREQLALIAGTAVVGVVLVLVVIVVAVLCLRKQSN
GREAEYSDKHGQYLIGHGTKVYIDPFTYEDPNEAVREFAKEIDVSYVKIEEVIGAGEFGEVCRGRLKAPGK
KESCVAIKTLKGGYTERQRREFLSEASIMGQFEHPNIIRLEGVVTNSMPVMILTEFMENGALDSFLRLNDG
QFTVIQLVGMLRGIASGMRYLAEMSYVHRDLAARNILVNSNLVCKVSDFGLSRFLEENSSDPTYTSSLGGK
IPIRWTAPEAIAFRKFTSASDAWSYGIVMWEVMSFGERPYWDMSNQDVINAIEQDYRLPPPPDCPTSLHQL
MLDCWQKDRNARPRFPQVVSALDKMIRNPASLKIVARENGGASHPLLDQRQPHYSAFGSVGEWLRAIKMGR
YEESFAAAGFGSFELVSQISAEDLLRIGVTLAGHQKKILASVQHMKSQAKPGTPGGTGGPAPQY (SEQ ID No.6)

FIG. 21C

GPX2 Sequence

A) Nucleic sequence

>gi|4504102|ref|NM_002083.1| Homo sapiens glutathione peroxidase 2 (gastrointestinal) (GPX2), mRNA

CGGCCTCTCTGCGGGGCTCACTCTGCGCTTCACCATGGCTTTCATTGCCAAGTCCTT
CTATGACCTCAGTGCCATCAGCCTGGATGGGGAGAAGGTAGATTTCAATACGTTCCG
GGGCAGGGCCGTGCTGATTGAGAATGTGGCTTCGCTCTGAGGCACAACCACCCGGGA
CTTCACCCAGCTCAACGAGCTGCAATGCCGCTTTCCCAGGCGCCTGGTGGTCCTTGG
CTTCCCTTGCAACCAATTTGGACATCAGGAGAACTGTCAGAATGAGGAGATCCTGAA
CAGTCTCAAGTATGTCCGTCCTGGGGGTGGATACCAGCCCACCTTCACCCTTGTCCA
AAAATGTGAGGTGAATGGGCAGAACGAGCATCCTGTCTTCGCCTACCTGAAGGACAA
GCTCCCCTACCCTTATGATGACCCATTTTCCCTCATGACCGATCCCAAGCTCATCAT
TTGGAGCCCTGTGCGCCGCTCAGATGTGGCCTGGAACTTTGAGAAGTTCCTCATAGG
GCCGGAGGGAGAGCCCTTCCGACGCTACAGCCGCACCTTCCCAACCATCAACATTGA
GCCTGACATCAAGCGCCTCCTTAAAGTTGCCATATAGATGTGAACTGCTCAACACAC
AGATCTCCTACTCCATCCAGTCCTGAGGAGCCTTAGGATGCAGCATGCCTTCAGGAG
ACACTGCTGGACCTCAGCATTCCCTTGATATCAGTCCCCTTCACTGCAGAGCCTTGC
CTTTCCCCTCTGCCTGTTTCCTTTTCCTCTCCCAACCCTCTGGTTGGTGATTCAACT
TGGGCTCCAAGACTTGGGTAAGCTCTGGGCCTTCACAGAATGATGGCACCTTCCTAA
ACCCTCATGGGTGGTGTCTGAGAGGCGTGAAGGGCCTGGAGCCACTCTGCTAGAAGA
GACCAATAAAGGGCAGGTGTGGAAACGGCAAAAAAAAAAAAAAAAAAAAAAAAAAA
AA (SEQ ID No.7)

FIG. 22A

B)GPX2 Protein Sequence:

>gi|4504103|ref|NP_002074.1| gastrointestinal glutathione peroxidase 2 [Homo sapiens]

MAFIAKSFYDLSAISLDGEKVDFNTFRGRAVLIENVASLXGTTTRDFTQLNELQCRF
PRRLVVLGFPCNQFGHQENCQNEEILNSLKYVRPGGGYQPTFTLVQKCEVNGQNEHP
VFAYLKDKLPYPYDDPFSLMTDPKLIIWSPVRRSDVAWNFEKFLIGPEGEPFRRYSR
TFPTINIEPDIKRLLKVAI (SEQ ID No.8)

FIG. 22B

hRGMR Sequence:

hCT18626:

ATGATAAGGAAGAAGAGGAAGCGAAGCGCGCCCCCCGGCCCATGCCGCAGCCACGGGCCCAGACCCGCCACGGCGCCCGCGCCGCC
GCCCTCGCCGGAGCCCACGAGACCTGCATGGACGGGCATGGGCTTGAGAGCAGCACCTTCCAGCGCCGCCGCTGCCGCCGCCGAGG
TTGAGCAGCGCCGCCGCCCCGGGCTCTGCCCCCCGCCGCTGGAGCTGCTGCTGCTGCTGCTGTTCAGCCTCGGGCTGCTCCACGCA
GGTGACTGCCAACAGCCAGCCCAATGTCGAATCCAGAAATGCACCACGGACTTCGTGTCCCTGACTTCTCACCTGAACTCTGCCGT
TGACGGCTTTGACTCTGAGTTTTGCAAGGCCTTGCGTGCCTATGCTGGCTGCACCCAGCGAACTTCAAAAGCCTGCCGTGGCAACC
TGGTATACCATTCTGCCGTGTTGGGTATCAGTGACCTCATGAGCCAGAGGAATTGTTCCAAGGATGGACCCACATCCTCTACCAAC
CCCGAAGTGACCCATGATCCTTGCAACTATCACAGCCACGCTGGAGCCAGGGAACACAGGAGAGGGGACCAGAACCCTCCCAGTTA
CCTTTTTTGTGGCTTGTTTGGAGATCCTCACCTCAGAACTTTCAAGGATAACTTCCAAACATGCAAAGTAGAAGGGGCCTGGCCAC
TCATAGATAATAATTATCTTTCAGTTCAAGTGACAAACGTACCTGTGGTCCCTGGATCCAGTGCTACTGCTACAAATAAGGCAAAG
GGTTACCCCGTTCTGCTTCCTTCCCATTCTGTTAAACCTTGTACATGCTCCTTCCCACAGATCACTATTATCTTCAAAGCCCACCA
TGAGTGTACAGATCAGAAAGTCTACCAAGCTGTGACAGATGACCTGCCGGCCGCCTTTGTGGATGGCACCACCAGTGGTGGGGACA
GCGATGCCAAGAGCCTGCGTATCGTGGAAAGGGAGAGTGGCCACTATGTGGAGATGCACGCCCGCTATATAGGGACCACAGTGTTT
GTGCGGCAGGTGGGTCGCTACCTGACCCTTGCCATCCGTATGCCTGAAGACCTGGCCATGTCCTACGAGGAGAGCCAGGACCTGCA
GCTGTGCGTGAACGGCTGCCCCCTGAGTGAACGCATCGATGACGGGCAGGGCCAGGTGTCTGCCATCCTGGGACACAGCCTGCCTC
GCACCTCCTTGGTGCAGGCCTGGCCTGGCTACACACTGGAGACTGCCAACACTCAATGCCATGAGAAGATGCCAGTGAAGGACATC
TATTTCCAGTCCTGTGTCTTCGACCTGCTCACCACTGGTGATGCCAACTTTACTGCCGCAGCCCACAGTGCCTTGGAGGATGTGGA
GGCCCTGCACCCAAGGAAGGAACGCTGGCACATTTTCCCCAGCAGTGGCAATGGGACTCCCCGTGGAGGCAGTGATTTGTCTGTCA
GTCTAGGACTCACCTGCTTGATCCTTATCGTGTTTTTGTAG

FIG. 23A

B. Protein Sequence:

hCP43057:

MIRKKRKRSAPPGPCRSHGPRPATAPAPPPSPEPTRPAWTGMGLRAAPSSAAAAAAEVEQRRRPGLCPPPLELLLLLLFSLGLLHA
GDCQQPAQCRIQKCTTDFVSLTSHLNSAVDGFDSEFCKALRAYAGCTQRTSKACRGNLVYHSAVLGISDLMSQRNCSKDGPTSSTN
PEVTHDPCNYHSHAGAREHRRGDQNPPSYLFCGLFGDPHLRTFKDNFQTCKVEGAWPLIDNNYLSVQVTNVPVVPGSSATATNKAK
GYPVLLPSHSVKPCTCSFPQITIIFKAHHECTDQKVYQAVTDDLPAAFVDGTTSGGDSDAKSLRIVERESGHYVEMHARYIGTTVF
VRQVGRYLTLAIRMPEDLAMSYEESQDLQLCVNGCPLSERIDDGQGQVSAILGHSLPRTSLVQAWPGYTLETANTQCHEKMPVKDI
YFQSCVFDLLTTGDANFTAAAHSALEDVEALHPRKERWHIFPSSGNGTPRGGSDLSVSLGLTCLILIVFL*

FIG. 23B

Sequences of Tspan 5:

A) Nucleic sequence

>gi|21264582|ref|NM_005723.2| Homo sapiens tetraspan 5 (TM4SF9), mRNA

CGCCTTTGCCCGAAGCCCGGGGACGAACCGACGGACCGACCGCCTGGCGCACGGACGCGGGCGCTCGCT
TTGTGTTCGGGGCTAGCGTCGGCGAGGCTTGAGCTTGCAGCGCGCGGCTTCCCTGCTTTCTCGCGGCCA
CCCCGGCTCCGGCGGCCTCGGCGCGCGAGGGGCTGGAGGTGCGGGAGCCGCTCTCCGCCGGTCGGTCCC
CGCGCGGCTGAGCCCAGGCCGCCAGCGCCGCGGCCCCGTGCGGTGTCCCTGAGCTCCTGCTCCCCGCCG
GGCTGCTCCGAGCAACGGTGCTTCGGAGCTCCAAACTCGGGCTGCCGGGGCAAGTGTCTTCATGAACCC
AGAGGATGTCCGGGAAGCACTACAAGGGTCCTGAAGTCAGTTGTTGCATCAAATACTTCATATTTGGCT
TCAATGTCATATTTTGGTTTTTGGGAATAACATTTCTTGGAATTGGACTGTGGGCATGGAATGAAAAAG
GAGTTCTGTCCAACATCTCTTCCATCACCGATCTCGGCGGCTTTGACCCAGTTTGGCTCTTCCTTGTGG
TGGGAGGAGTGATGTTCATTTTGGGATTTGCAGGGTGCATTGGAGCGCTACGGGAAAACACTTTCCTTC
TCAAGTTTTTTTCTGTGTTCCTGGGAATTATTTTCTTCCTGGAGCTCACTGCCGGAGTTCTAGCATTTG
TTTTCAAAGACTGGATCAAAGACCAGCTGTATTTCTTTATAAACAACAACATCAGAGCATATCGGGATG
ACATTGATTTGCAAAACCTCATAGACTTCACCCAGGAATATTGGCAGTGCTGTGGGGCTTTTGGAGCTG
ATGATTGGAACCTAAATATTTACTTCAATTGCACAGATTCCAATGCAAGTCGAGAGCGATGTGGCGTTC
CATTCTCCTGCTGCACTAAAGATCCCGCAGAAGATGTCATCAACACTCAGTGTGGCTATGATGCCAGGC
AAAAACCAGAAGTTGACCAGCAGATTGTAATCTACACGAAAGGCTGTGTGCCCCAGTTTGAGAAGTGGT
TGCAGGACAATTTAACCATCGTTGCTGGTATTTTCATAGGCATTGCATTGCTGCAGATATTTGGGATAT
GCCTGGCCCAGAATTTGGTTAGCGATATCGAAGCTGTCAGGGCGAGCTGGTAGACCCCCTGCAACCGCT
GCTGCAAGACACTGGACAGACCCAGCTTTCGGGACCCTCCCGCGTGCCGAACTGATCTTCGAGCTGCAT
GGACCTAATCACAGATGCAGCCTGCAGTCTCGCCTAATGGAGCTGCCATTAGGGGAGTGTAAAACTGGG
AAATGCTGCTCACTGACAGAATTAAAAAAAAAAATAACCAGTATGAAAGTCGTTGCGCCGTGAATCTCT
ACTGTAGCCATGAATTTATGGACAGTTAGATGCTTACCAAAAAAGAAAAAAAA (SEQ ID No.11)

FIG. 24A

B) Protein Sequence of Tspan5:

>gi|21264583|ref|NP_005714.2| (NM_005723) tetraspan 5; tetraspan TM4SF; tetraspan NET-4; transmembrane 4 superfamily member 9; transmembrane 4 superfamily, member 8; tetraspanin 5 [Homo sapiens]

MSGKHYKGPEVSCCIKYFIFGFNVIFWFLGITFLGIGLWAWNEKGVLSNISSITDLGGFDPVWLFLVVG
GVMFILGFAGCIGALRENTFLLKFFSVFLGIIFFLELTAGVLAFVFKDWIKDQLYFFINNNIRAYRDDI
DLQNLIDFTQEYWQCCGAFGADDWNLNIYFNCTDSNASRERCGVPFSCCTKDPAEDVINTQCGYDARQK
PEVDQQIVIYTKGCVPQFEKWLQDNLTIVAGIFIGIALLQIFGICLAQNLVSDIEAVRASW (SEQ ID No.12)

FIG. 24B